THE DIAGNOSIS OF PANCREATIC DISEASE

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With a Foreword by
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Foreword

The advances of the last twenty years in the therapy of pancreatic lesions have emphasized the importance of accurate diagnosis and valid diagnostic tests. Fasting and blood-sugar determinations with levels below 50 mg. per cent have proved to be the most important laboratory tests in islet-cell tumors. Similarly, elevated serum amylase findings have been of the greatest help in the diagnosis of acute pancreatitis.

In the obstructive lesions of the head of the pancreas and of the ampullary area, insufficient attention has been paid in this country to the work of the Stockholm school in developing duodenal intubation to determine the acinar activity of the pancreas.

Dr. Bauman's experience during the past twenty-five years in the study of metabolic disease and pancreatic lesions, in association with the medical and surgical services at the Columbia-Presbyterian Clinic, eminently qualify him in his analysis of the large mass of clinical and laboratory data in these fields. His management is based upon carefully checked and followed clinical histories. It gives this writer great satisfaction to see these data analyzed and to have had the privilege of associating with Dr. Bauman in the study and the care of so many of the patients reported.

This is a much-needed monograph and should stimulate further studies in the clinics of this country in pancreatic disease.

ALLEN O. WHIPPLE, M.D.

Preface

During the last 20 years, three contributions have especially advanced our knowledge of the pancreas and its diseases.

Starting with the preparation of secretin almost fifteen years ago, Agren, Hammarsten, Berglund, Lagerloef, and associates of the Stockholm school gradually developed a practical test of external pancreatic function. After the intravenous injection of the hormone, a dilute pancreatic secretion was aspirated from the duodenum with a specially constructed double tube. In this way, admixture of gastric secretion was avoided. A compilation of this work by H. O. Lagerloef entitled *Pancreatic Function and Pancreatic Disease* was published about six years ago. The author is pleased to acknowledge the help and the inspiration that he received from this book, which is a lasting contribution to the diagnosis of pancreatic disease.

The medical world is also indebted to Robert Elman, of Washington University, St. Louis, for demonstrating the value of the serum amylase test in the diagnosis of acute pancreatitis.

Further tribute is due Dr. A. O. Whipple and his associates for progress in the surgery of the pancreas. This pioneer work has enabled surgeons to remove part or all of the organ in certain cases of hyperinsulinism, chronic pancreatitis and carcinoma. For the first time it was possible to observe the effects of the complete removal of the pancreas on human beings.

In this monograph the writer has attempted to correlate the laboratory and clinical experience in pancreatic disease at the Presbyterian Hospital, New York, during the past ten years. For reasons to be discussed, the vagus stimulant mecholyl, was chosen to provoke pancreatic secretion. About 550 determinations were made on patients suffering from pancreatic and nonpancreatic disease.

LOUIS BAUMAN, M.D.

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Mrs. Donald J. Huyssoon prepared the manuscript.

Louis Bauman, M.D.

Contents

Abbreviations

Ac. = Acute
C.B.D. = Common bile duct
Chr. = Chronic
Ca. = Carcinoma
Diab. = Diabetic
Duod. = Duodenum
D.U. = Duodenal ulcer
F.U. = Follow-up
G.B. = Gallbladder
G.T.T. = Glucose tolerance test
Hd. = Head
J. = Jaundice
l. = Low
P. = Pancreas
Pctis. = Pancreatitis
P.D. = Pancreatic duct
P.F.T. = Pancreatic function test
S.A. = Serum amylase

Introduction

The purpose of this publication is to discuss the pancreatic function tests and their application in the diagnosis of pancreatic disease.

Although the pancreas is the principal organ that is concerned with the digestion of starch, protein, and fat, an appraisal of its functional capacity was impractical until a few years ago. Recent progress in the surgery of the pancreas and the introduction of new laboratory methods have advanced our knowledge of this organ in health and disease.

The need for a measure of acinar activity of the pancreas has long been apparent. Such a test should aid in diagnosing the cause of obstructive jaundice, steatorrhea, and other abdominal conditions. Clinicians are therefore indebted to Agren, Hammarsten, Lagerloef, and associates[1-6] for developing a practical pancreatic function test. The results of the Swedish investigators have been confirmed in this country by Diamond and Siegal, Comfort and Osterberg, Pratt, Lake, and others.[7-16]

Accurate determination of pancreatic ferment activity requires experience and familiarity with the properties of these remarkable high molecular catalysts. For example, considerable time was lost before the importance of collecting the pancreatic secretion in iced containers was realized. This was necessary to avoid reduction in ferment activity. On the other hand, the quantitative estimation of the end products of ferment activity, that is, reducing sugar, nonprotein nitrogen, and butyric acid, is fairly simple and commonplace.

The serum amylase determination has been generally accepted as a means of differentiating acute pancreatitis from the other more common abdominal emergencies such as perforated duodenal ulcer, acute biliary tract conditions, acute appendicitis and intestinal obstruction. It seems probable that its usefulness will be extended in the future.

According to Comfort and Osterberg,[17] serum ferment estimation is valuable in acute pancreatitis, carcinoma of the pancreas, and in

chronic pancreatitis as long as the inflammatory process is active and acinar tissue remains. In carcinoma, serum lipase was elevated in 28 of their 69 cases (40.5%), and serum amylase in 2 of 25 cases (8%).

Fat absorption studies are helpful when the pancreatic juice is not obtainable for one reason or another. When fat absorption is inadequate, the effect of pancreatic preparations by mouth may be ascertained in this way.

The astonishingly good fat absorption noted at times in the absence of pancreatic juice is unexplained. Thanks to the pioneer work of A. O. Whipple and followers,[18,19] the human pancreas is no longer considered an indispensable organ. It seems likely that more lives will be saved or made endurable as progress in the diagnosis and treatment of pancreatic disease continues. With the aid of commercial insulin and dried pancreas preparations, a depancreatized person may be maintained on an appropriate, balanced diet in a fair state of health.[20,21,22]

The mildness of the diabetes in depancreatized individuals was unexpected and is difficult to explain. Animal experimentation suggests that the pancreas produces an insulin-inhibiting agent. For example, an alloxan diabetic dog under comparable conditions requires more insulin before than after his pancreas has been removed.[23] Most recently, Heard and coworkers obtained a fraction from pancreatic extract that lowered liver glycogen and raised the blood sugar.[24]

PART I

Pancreatic Function Test

In 1926, Chiray and his associates[24] studied the action of purified secretin, a protein hormone extracted from the mucous membrane of the small intestine, on the external secretion of the human pancreas. After duodenal intubation, 0.03 Gm. of the product was injected intravenously. A definite increase in volume, protease, and lipase resulted. Ten years later, Chiray and Bolgert[25], using a commercial secretin preparation*, noted a diminished output of ferments in verified subacute pancreatitis and carcinoma. Later, in 1939, these authors extended their clinical studies.

We are indebted to W. Hammarsten, E Agren, H. Lagerloef and their associates[1-6] for improving the technic and thus furnishing a practical method of testing the external secretion of the pancreas.

At first a purified secretin was prepared; this, however, was too expensive for routine clinical use. A suitable commercial preparation was then developed†. Following its intravenous injection into a normal person, an average of 136 cc. of dilute pancreatic juice was secreted in ½ hour. When a satisfactory stimulant had been discovered the next problem was to prevent admixture of the pancreatic secretion with gastric juice, for it is well known that pancreatic enzymes are destroyed in an acid medium. The use of a conjoined double tube with the longer end entering the duodenum and the shorter end terminating in the stomach, permitted the separate aspiration of the two organs with minimal escape of acid into the duodenum.

The results are discussed by H O. Lagerloef[6] A comparison of the volume, bicarbonate, and ferment content of the secretion in pancreatic and nonpancreatic diseases demonstrated the diagnostic value of the test. Diamond and Siegel[7,8] confirmed these results in this country. They were impressed by the dilute character of the secretion after secretin in-

*Hormoduodenine, prepared by Maison Bila

†Astra Laboratories of Soedertalje, Sweden

jection as contrasted with the more concentrated juice after vagal stimulants. These authors also noted that in pancreatic disease the enzyme production was first affected. Comfort and Osterberg[9] confirmed the difference in volume after the two types of stimulation. The average ten-minute volume before stimulation was from 7 to 8 cc. After secretin, 120 cc. of juice was aspirated in forty minutes, while after mecholyl* (vagus stimulant), an average of only 50 cc. was obtained (see Fig. 1). They conclude, "the increase in total ferments appeared to be due to a washing-out process in the case of secretin and to an active secretion of

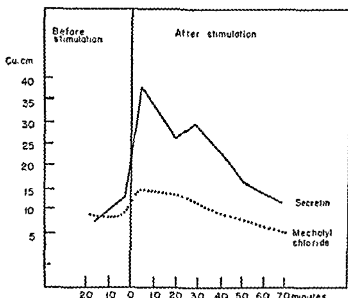


Fig. 1. Average volume of duodenal contents per unit of time before and after stimulation with secretin and mecholyl chloride. (Comfort, M. W., and Osterberg, A. E.: Arch Int. Med. 66:688.)

enzymes in the case of mecholyl . . . *the concentration of ferments with mecholyl may prove to be a more reliable index of pancreatic function than the total values per unit of time after stimulation with either secretin or mecholyl.*"

In a case of recurrent pancreatitis, Comfort[10] found that both secretin and mecholyl produced an abnormal increase in volume, a hyposecretion of amylase, and a hypersecretion of protease and lipase. This dissociation had been noted by previous workers.[7,8] In advanced pancreatitis, all ele-

*Mecholyl chloride is the trade name for acetyl beta methylcholine chloride. Its properties are described in the J.A.M.A., 124:860, 1941.

ments were below normal. He believes that both mecholyl and secretin are powerful stimulants and that foods are less so. Necheles[27] noted that the commercial secretin preparation deteriorated and became toxic on standing.

For the aforementioned reasons and because secretin was expensive or impossible to obtain, we used mecholyl as the pancreatic stimulant.

A Miller-Abbott type of rubber tube 4 feet long and 16 french, divided into two longitudinal compartments by a central partition, was used. The duodenal end is provided with a perforated metal tip. The

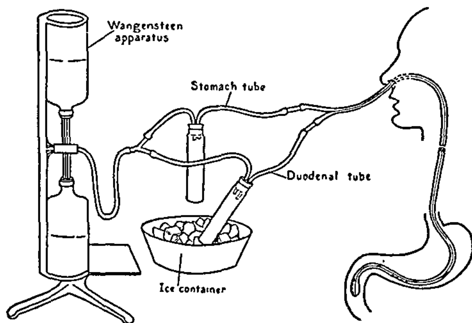


FIG. 2. The arrangement of the apparatus for the pancreatic function test. (Bauman, L.: Tests of the external pancreatic function, Nelson's New Loose Leaf Surgery, vol. 5, New York, Nelson, pp. 423-428.)

gastric canal is perforated where it is in contact with the stomach wall; it has no connection with the duodenum. The tube is passed through the nose into the stomach (see Fig. 2) [26] This is best done the night before but may be inserted in the fasting state on the morning of the test. The patient rests on the right side, and the tube is manipulated into the duodenum under the fluoroscope by the roentgenologist. This may be difficult, time-consuming, or impossible. Pylorospasm, adhesions about the duodenum, or abnormal or unusual conformation of the stomach or duodenum may be the cause of failure. In several instances, 0.015 Gm.

morphine hypodermically has enabled the passage of the tube into the duodenum. After the tube is in the duodenum, it is taped to the nose with adhesive plaster, and 10 cc. of a 25 per cent emulsion of finely powdered calcium carbonate in gum acacia solution is syringed into the stomach to neutralize excess acid. This must be repeated if the pancreatic juice fractions continue to be acid. The oral ends are joined to the receiving test tubes into which the juices are aspirated by constant gentle suction by means of a Wangensteen apparatus. The duodenal glass receiving tube must be iced to avoid destruction of ferments during collection. After obtaining the first ten-minute sample, 0.010 of mecholyl chloride is injected subcutaneously. Ten, 20, and 30 minutes later, three further ten-minute fractions are collected. The fractions are preserved in ice until analyzed. The *p*H is determined with a Hellige *p*H meter. If the specimen is neutral or alkaline, its volume, amylase, protease and lipase concentrations are determined.

It is suggested that a solution of atropine sulfate for hypodermic injection be at hand to anticipate undue sensitivity to the vagomimetic drug. Especial care in asthma and heart disease is advisable. However, we have had very little trouble in this respect in over five hundred cases.

Before publication of the Free and Myers[28] method, the concentration of ferments was determined by noting the least amount of juice required for active digestion of substrate. The amylase was estimated according to Wohlgemuth,[29] the protease according to Gross,[30] and the lipase according to Cherry and Crandall.[31] The ferment activity was expressed as active (+), low (1), or absent (0).

For optimum results with the more recent Free and Myers method, a mechanical shaker is desirable. For the determination of lipase, tributyrin, advocated by Free and Myers, gives more uniform results than emulsified olive oil. (Compare Tables 1 and 2). The range of values was from 4 to 21 cc. with tributyrin, and from 2 to 61 cc. with emulsified olive oil.

The steps that are necessary to obtain four alkaline fractions and to determine their hydrogen ion and ferment concentrations consume the better part of a laboratory day. This expenditure of time may be shortened as experience increases. At any rate, the test promises to become a routine procedure in the hospital chemical laboratory.

In this publication, an attempt has been made to correlate the results of approximately 550 pancreatic function tests with other

TABLE 1. LIPASE VALUES IN NONPANCREATIC DISEASE USING AN EMULSIFIED OLIVE OIL SUBSTRATE*

Fractions Cc. 0.1 Normal Acid				Diagnosis and Remarks
1†	2	3	4	
	19	23	18	Stones in gallbladder—cholecystectomy
23	19	23	17	
9	40	44	42	Stones in common bile duct—jaundiced
0.7	24	24	15	Normal Control
12	25	28	17	Lymphosarcoma
5	30	19	17	Cirrhosis of liver—biopsy pancreas = negative
	15	15	13	Ca gallbladder—peritoneal metastases
	4	8	9	Hanot's cirrhosis—explored
4	17	15	14	Biliary cirrhosis—unoperated
8	19	2	4	Control
2		11	37	Ca stomach at operation
	35	20	38	Psychoneurosis—diarrhea
	0.3	16	30	Control
8	2	14	22	Control
10	2	14	13	Ca lymph gland
3	25	29	0.5	Ca. colon
1	28	5	5	Exploration—undiagnosed
6	33	6	6	Control
0.2	29	43	74	Catarrhal jaundice or hepatitis
0.4	23	49	0.4	{Exploration—biopsy pancreas = normal
17	39	48	52	}Repeated 1 month later
2	1	41	2	Ulcer heel
2	23	9	7	Control
4	52	58	98	Control
40	27	8	54	Control
3	15	24	28	Hepatitis
53	74	61	25	Stone in common bile duct
36	97		79	Stones in gallbladder—cholecystectomy
0.6	8	58	33	Cholesterosis, operated
22	58	36	0.5	Cholecystectomy
	41	18	45	Stricture of common bile duct
27	50	36	28	Stones in gallbladder
3	34	34	33	Stone in common bile duct—pancreas felt normal
0.1	20	18	0.7	Psychoneurosis

*The amylase and protease values were normal in all cases
†Fraction 1 obtained during the ten minutes before mecholyl was injected

laboratory and clinical data and with the findings at operation and/or autopsy.

In this connection, it is well to recall the large functional reserve of the pancreas. A minimal amount of healthy tissue can produce a normal pancreatic juice. Furthermore, the nervous influence on pancreatic secretion must not be overlooked. An abnormal juice may indicate autonomic imbalance rather than parenchymal disease.

TABLE 2. LIPASE VALUES IN NONPANCREATIC DISEASE, USING TRIBUTYRIN AS A SUBSTRATE*

Fractions 0.1 N Butyric Acid 1†	2	3	4	Diagnosis and Remarks
13	16	11	13	Ca. of the stomach
10	14	12	15	Stone in common bile duct—P. felt normal
	16	14	7	Ca. of the stomach
12	13	17	11	Arsphenamine hepatitis
	13	11	15	Hepatitis
10	19	19	17	Undiagnosed—unoperated
12	17	16	14	Stones in gallbladder—P. felt normal
14	15	17	16	Common bile duct obstruction by adhesions or enlarged glands—P. felt normal
14	18	17	15	Anxiety neurosis
13	14	14	15	Renal calculi—autopsy
11	16	24	16	Control—unoperated
11	17			Cholangitis
13	21	22	15	Ca. of lung
13	18	15		Stones in gallbladder—cholecystectomy
13	17	16	15	Stones in gallbladder—neighboring organs normal
12	16	16	15	Cerebral thrombosis—unoperated
14	21	18	17	Undiagnosed
15	14	15		Regional ileitis
14	15	14	16	Stones in common bile duct and gallbladder—P. = normal
12	13	12	13	Fistula between gallbladder and duodenum
12	18	16	11	Duodenal ulcer
16	17	16	16	Unoperated—undiagnosed
13	18	19	16	Unoperated
2	4	18		Cicatricial stenosis common bile duct
14	16	13	12	Undiagnosed

*Amylase and protease values were normal in all patients.
†Fraction 1 was obtained during ten minutes before mecholyl injection

The estimation of pancreatic ferments in cyst or fistula fluids can assist the surgeon in determining the nature of an abdominal cyst and in the diagnosis of pancreatic fistulae.

The results of the ferment determinations are expressed as follows:

Amylase activity = mg. of glucose liberated from starch by 0.001 cc. of pancreatic juice.

Protease activity = mg. of amino nitrogen liberated from casein by 1 cc. of pancreatic juice.

Lipase activity = the amount of 0.1 N. butyric acid liberated by 0.1 cc. of pancreatic juice.

The accuracy of the test is affected by the unknown dilution with gastric, hepatic, and duodenal secretions and by the variable response of the pancreas in different people to the same stimulus. This is comparable with the behavior of the stomach after histamine injection.

As will be seen, the pancreas, in common with the liver and other organs, has a large measure of functional reserve. Most of its parenchyma must be laid low before a discernible decrease in ferment concentration is demonstrable. However, in spite of these disturbing limitations, experience has shown that the procedure yields information which is of definite clinical value. For example, by demonstrating lessened ferment activity in the pancreatic juice, Andersen[32] showed that certain cases of celiac disease were actually due to pancreatic fibrosis.

THE FUNCTIONAL RESERVE OF THE PANCREAS

The following clinical reports demonstrate the remarkable functional activity of a small remnant of the organ.

Z. G., history number 512939, a woman of 45, was admitted in February, 1937, for attacks of unconsciousness and with a fasting blood sugar of 26 mg. per cent. The symptoms were prevented by food. At operation a subtotal pancreatectomy was done because an island-cell tumor could not be found. In the resected specimen, a small nodule in the tail of the pancreas proved to be an adenoma of the islands of Langerhans. *Six months later, she was readmitted for increasing hunger. She* had gained 30 pounds. The fasting blood sugar was 48; one month later it was 30. At the second operation, the remaining pancreatic tissue was smaller than expected; it measured 4 x 3 x 2 cm. When the duodenum was mobilized, a nodule was felt close to the papilla of Vater. It was removed. It proved to be another adenoma of the islands of Langerhans. During the 11 years that followed, she has had no further symptoms of hypoglycemia, and her fasting blood sugars have been normal.

Glucose Tolerance Test after 100 Grams of Glucose

	Fasting	*½ hr.*	*1 hr.*	*2 hr.*	*3 hr.*	*4 hr.*	*5 hr.*	*6 hr.*
March 1938	95			167	142	70	76	84
June 1940	90	166	178	133	127			

With only a small remnant of the pancreas, this woman had no symptoms of diabetes and an almost normal glucose tolerance test. Apparently

TABLE 2. LIPASE VALUES IN NONPANCREATIC DISEASE, USING TRIBUTYRIN AS A SUBSTRATE*

FRACTIONS 0.1 *N Butyric Acid*				DIAGNOSIS AND REMARKS
1†	*2*	*3*	*4*	
13	16	11	13	Ca. of the stomach
10	14	12	15	Stone in common bile duct—P. *felt* normal
	16	14	7	Ca. of the stomach
12	13	17	11	Arsphenamine hepatitis
	13	11	15	Hepatitis
10	19	19	17	[illegible]
12	17	16	14	[illegible]
14	15	17	16	[illegible] lhesions or enlarged glands—P. *felt normal*
14	18	17	15	Anxiety neurosis
13	14	14	15	Renal calculi—autopsy
11	16	24	16	Control—unoperated
11	17			Cholangitis
13	21	22	15	Ca. of lung
13	18	15		Stones in gallbladder—cholecystectomy
13	17	16	15	Stones in gallbladder—neighboring organs normal
12	16	16	15	Cerebral thrombosis—unoperated
14	21	18	17	Undiagnosed
15	14	15		Regional ileitis
14	15	14	16	Stones in common bile duct and gallbladder—P. = normal
12	13	12	13	Fistula between gallbladder and duodenum
12	18	16	11	Duodenal ulcer
16	17	16	16	Unoperated—undiagnosed
13	18	19	16	Unoperated
2	4	18		Cicatricial stenosis common bile duct
14	16	13	12	Undiagnosed

*Amylase and protease values were normal in all patients.
†*Fraction 1 was obtained during ten minutes before mecholyl injection*

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stedt,[34] from his experience with dogs, thinks that removal of from 80 to 90 per cent of the pancreas causes no defect in carbohydrate metabolism or in the absorption of food stuffs. These facts suggest that in clinical cases, low ferment concentration in the pancreatic juice indicates extensive destruction of parenchyma. This is not always true, however.

Greatly lowered function may be unassociated with morphologic change, nor does identical pancreatic pathology invariably produce the same functional disturbance. To quote Professor V. Kneeland Frantz,[35] "In both benign and malignant tumors of islet-cells there are no histologic criteria by which we can distinguish those which are functional and those which are not. With an exceedingly small adenoma, a patient may be unconscious from hypoglycemia while with an even larger similar tumor in another case there may be no symptoms of hyperinsulinism."

FERMENT DEFICIENCY WITHOUT MORPHOLOGIC CHANGE

The following is an example of greatly lowered functional activity without morphologic change.

M. M., a man of 48, history number 699889, complained of nausea, vague right upper quadrant and epigastric pain for two years and a weight loss of 30 lbs. Physical examination, glucose tolerance test, cholecystogram, roentgenogram of the stomach and intestine, were normal. The serum amylase was 33, and there was no acid in the stomach after histamine. The pancreatic function test was abnormal.

PANCREATIC FUNCTION TEST

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Volume. . .	7	25	15	8
*p*H.. . .	7.5	7.5	7 5	7 5
Amylase	low	low	low	low
Protease	low	low	low	low
Lipase. ..	. .. 3.0	3 0	3 0	3 0

At operation, the surgeon thought that the pancreas was harder than normal and suggested cancer. A partial resection was done, but histological examination of the specimen was normal. He was followed for three years. He felt well and gained 20 pounds.

Another somewhat similar case was P. L , history number 818088, an

enough insulin was produced to meet the ordinary metabolic demands. What about the ferment production by the alveolar cells?

A pancreatic function test in December, 1946, gave the following results:

	Fraction 1 *Before Mecholyl*	Fraction 2 *10 min. p. mech.*	Fraction 3 *20 min. p. mech.*	Fraction 4 *30 min. p. mech.*
*p*H.......	7.4	7.4	7.4	7.4
Color . .	golden yellow	brown-yellow	brown-yellow	golden yellow
Amylase. .	11.3 mg.	11.8	12.3	8.4
Protease...	113. mg.	134.	141.	71.
Lipase....	15.5 cc.	16.1	16.5	14.3
Bile......	moderate amount	large amount	large amount	moderate amount

The concentration of ferments in the pancreatic juice was normal.

The following experience affords further evidence of the high functional activity of a small remnant of pancreatic tissue.

Mrs. H. S., history number 679309, aged 46, was explored for spells of unconsciousness associated with a blood sugar of 46 mg. per cent. No pancreatic tumor was found. Owing to technical difficulties, the contemplated pancreatectomy had to be abandoned. Symptoms of hyperinsulinism and low blood sugars persisted. At the second operation four years later, what appeared to be the entire pancreas was removed. The surgeon stated, however, that there was a possibility that a small tab of pancreatic tissue remained. The excised organ weighed 54 grams and was 15 cm. long. An islet-cell tumor was found in the substance of the gland. *Soon after operation, blood sugars of 195, 192 and 176 were noted.* During the following ten months, she had no symptoms. The blood sugar three hours after breakfast was 65 mg. per cent. One year after operation, the fasting blood sugar was 95 mg. per cent. The blood sugars one, two and three hours after 100 grams of glucose by mouth were 163, 192 and 86, respectively. Two years after operation, a pancreatic function test revealed the presence of all three ferments in the pancreatic juice. *Unfortunately, only one alkaline fraction was obtained, but this* contained 2.1 amylase, 113 protease and 6.5 lipase. The fasting blood sugar now, two years after pancreatectomy, is 92 mg. per cent.

In cystic fibrosis of the pancreas in infants, Andersen[32] observed that symptoms were absent unless 90 per cent of the organ was involved. In a dog, Coffey, Mann and Bollman[33] found that a nodule weighing 1/40 of the normal gland maintained normal pancreatic function. Drag-

The wide range of values results from unavoidable sources of error previously mentioned, namely, the variable individual response to mecholyl and the unknown dilution by other secretions. In the circumstances, the highest fractional value indicates the best functional activity.

Ninety-two per cent of the amylase values were above 4 mg. of reducing sugar; 96 per cent of the protease values were above 50 mg. of nonprotein nitrogen, and 96 per cent of the lipase values were above 8 cc. of 0.1 normal acid.

TABLE 3. THE FERMENT CONCENTRATION OF THE PANCREATIC JUICE IN NONPANCREATIC DISEASE

AMYLASE *Mg. reducing sugar*				PROTEASE *Mg. nonprot. N.*				LIPASE *cc. n/10 acid*				DIAGNOSIS
Fractions				Fractions				Fractions				
1	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	
6	6	7	2	177	181	255	100	16	17	22	16	Stones gallbladder—Unoperated
2	6	2	5					15	18	16	18	*Stone in gallbladder—Operated*
6	9		8	108	180		168	15	17		15	Unoperated
4	10	6	8	67	146	199	177	14	17	18	17	Stones gallbladder and common bile duct—P. = normal
5	6	12	6	116	147	304	147	17	17	20	18	Unoperated
4	8	9	8	59	214	106	59	12	15	13	12	Lymphosarcomatous cervical gland
3	8	9	4	39	127	148	165	8	14	7	14	Unoperated
3	7	6	4	35	182	106	98	11	16	15	15	*Unoperated—probably gallstones*
10	11	19	13	134	176	252	185	15	17	18	18	Unoperated
2	11	10	11					8	17	15	16	Cicatricial stenosis common bile duct
6	14	2	3					14	16	13	12	Unoperated
	18	11	10						15	13	13	Exploration P. = normal Cholangiolitis
6	9	7	11	101	182	120	95	14	14	15	12	Unoperated
10	14	17		108	158	181			15	16	16	Unoperated
4	10	11	6	60	181	146	42	13	15	13	13	Unoperated
	18	18	17		189	155	56		15	13	12	Unoperated
	6	15	7						15	15	16	Hepatitis
10	13	13	13	77	95	389	81	13	14	14	12	Retroperitoneal tumor
	14	12	12		231	199	221		16	16	18	Unoperated
3	10	16			216	193	195	14	16	14	15	Unoperated
4	9	8		137	300	168		14	16	16		Unoperated
4	18	13	8	274	236	509	584	14	15	14	17	Unoperated
7	14	15	14	35	35	405	519	8	17	17	13	Unoperated—nervous diarrhea
2	4	9		61	165	314		4	15	16		Stone in common bile duct
4	5	11	6	89	90	109	118	11	11	13	13	Ca transverse colon
8	13	17	16	143	194	146	152	12	13	12	11	Unoperated—melancholia
6	6	7	7	285	238	350	315	11	12	11	11	Unoperated—hepatitis

unmarried girl of 31 with a typical history of gallbladder disease but with a normal roentgenogram of the gallbladder and gastro-intestinal tract except for moderate pylorospasm. Serum amylase was normal.

PANCREATIC FUNCTION TEST—MAY 17, 1946

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Volume.....	44	80	56	28
*p*H..........	7.0	7.1	7.1	7.1
Amylase.....	1.0	13.0	10.0	.3
Protease.....	11.0	42 0	20.0	14 0
Lipase	2 0	3 0	2.0	2.0

PANCREATIC FUNCTION TEST—JULY 5, 1946

	Fraction 1	*Fraction 2*	*Fraction 3*	*Fraction 4*
Volume......	38.0	26.0	24.0	25.0
*p*H..........	7.3	7.3	7.3	7.3
Amylase.....	3 0	15.0	15.0	15 0
Protease.....	29.0	20.0	238.0	218 0
Lipase.......	4.0	4.0	6.0	6.0

On 6/4/46, the serum amylase was 36 (minimal normal values: amylase 4, protease 50, lipase 8).

No abnormalities were found at exploratory laparotomy.

Both of these patients suggested a psychosomatic disorder. Was there an abnormal vagus influence?

FERMENT CONCENTRATION OF PANCREATIC JUICE

NONPANCREATIC DISEASE

Volume. See Table 4.

The volume of each of the four alkaline ten-minute fractions was determined in 169 nonpancreatic patients. It varied widely both before and after mecholyl injection, yet in 82 per cent it was below 30 cc. The mean and median values were higher in the second and third fractions than in the others. The mean for all fractions was 18.6 cc. Comfort and Osterberg[9] determined the ten-minute volume after mecholyl in eight normal subjects. It averaged 13.6 cc.

Reaction. The *p*H of the pancreatic juice after mecholyl was between 7 and 8. Acid fractions were discarded.

Ferment Concentration. The ferment concentrations in nonpancreatic diseases are tabulated and charted. (See Table 3, Figs. 4-6.)

TABLE 3 (*Continued*). THE FERMENT CONCENTRATION OF THE PANCREATIC JUICE IN NONPANCREATIC DISEASE

AMYLASE *Mg. reducing sugar* Fractions				PROTEASE *Mg. nonprot. N.* Fractions				LIPASE *cc. n/10 acid* Fractions				DIAGNOSIS
1	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	
6	15	14	7	89	155	45	59	10	16	8	6	Unoperated
3	13	11	21	64	239	342	104	16	25	26	18	Chronic enteritis
	8	6	4		321	212	176		16	16	14	Unoperated
6	8	7	7	221	336	239	277	15	19	16	17	Unoperated
	16	18	15		319	373	248		18	20	17	Unoperated
11	11	11	11	114	97	110	80	14	14	14	14	Stone common bile duct—P. = normal
	6	5	5		47	92	84		10	30	9	Unoperated
11	12	12	8	112	134	141	71	15	16	17	14	Hyperinsulinism, partial pancreatectomy
	15	15	7		160	136	16		17	18	3	Unoperated
4	6	10	10	70	108	203	269	17	17	20	20	Enteritis, sprue
3	9	6	4	47	134	114	63	8	15	10	9	Hepatitis
6	11	9	7	193	279	238	224	12	24	17	10	Stones in gallbladder—cholecystostomy
4	14	14	9	67	276	281	154	4	17	16	14	Stone common bile duct—P. felt normal
12	12	12	12	7	122	108		1	11	13		Unoperated
5	15	10	9	53	91	63	61	9	12	13	13	Cicatricial stenosis common bile duct
6	11	10		91	308	101		15	18	15		Stones in gallbladder and common bile duct
3	12	9	10					13	15	14	14	Stones in common bile duct
7	10	9	16					12	18	18	17	Retroperitoneal sarcoma
14	14	14	14	110	378	188		9	21	18		Hepatitis
12	12	12	12		288	383	278	17	16	16	15	Diarrhea
5		7		58		265		15		18		Cirrhosis
9	8	14	8	126	147	196	107	16	17	18	17	Unoperated
	7	7	6	37	266	272	182	7	19	19	18	Diarrhea
7	10	10	10	101	237	242	199	14	18	17	16	Hepatitis
1	6	6		45	105	109		12	16	14		Psychoneurosis
6	16	14	9	141	287	273	192	9	14	12	11	Unoperated
18	19	19	19	147	271	293	208	21	18	18	17	Unoperated
5	6	6	6	60	103	94	90	6	9	9	8	Stones in gallbladder
10	10	10	10	157	226	152		15	18	18		Stones in gallbladder and common bile duct
3	11	5	3	62	191	104	67	11	15	12	11	Duodenal ulcer
2	2	6	6	62	63	99	151	12	11	13	16	Anorexia nervosa

TABLE 3 (*Continued*). THE FERMENT CONCENTRATION OF THE PANCREATIC JUICE IN NONPANCREATIC DISEASE

AMYLASE *Mg. reducing sugar*				PROTEASE *Mg. nonprot. N.*				LIPASE *cc. n/10 acid*				DIAGNOSIS
Fractions				Fractions				Fractions				
1	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	
2	3	16	16	15	33	116	116	1	2	17	19	Ca. adrenal
2	14	14	14	50	426	186	267	7	17	13	13	Unoperated—stones in gallbladder
7	8	10	10	132	353	482	454	10	12	10	11	Stones in common bile duct
2	6	6	6	88	287	343	301	8	14	14	13	Unoperated
3	16	16	16	15	279	458	388	6	8	15	15	Unoperated
9	18	16	8	168	197	320	283	10	10	10	10	Unoperated
	12	15	14		236	227	233		15	14	14	Hepatitis
12	21	15	11	120	195	173	122	9	13	12	10	Diverticulum esophagus
11	15	20	24	20	56	86	133	3	9	12	14	Unoperated
10	12	14	14	79	243	105	151	12	16	14	15	Stone in common bile duct
4	4	9	4	28	148	91	72	2	10	5	6	Cirrhosis, Laennec
14	14	14	14	203	272	235	291	14	15	14	15	Ca. of stomach
6	9	7		96	165	87		6	15	12		Ca liver
3	10	8	4	69	214	207	53	7	17	12	8	Unoperated
1	6	6	4	16	130	134	87	10	14	15	11	Unoperated
2	6	5	1	50	300	14	50	5	15	4	1	Unoperated
8	13	13	15	138	210	215	219	11	14	14	14	Glomerulonephritis
5	14	13	15	28	171	156	126	5	13	14	13	Ca. stomach
4	12	11	6	87	132	164	101	7	10	12	10	Unoperated
1	4	5	3	34	115	146	141	5	11	12	11	Cirrhosis liver
	9	9			84	79			11	11		Stones gallbladder and common bile duct—P. = normal
	2	7	9		84	19	176		13	5	15	Unoperated
	3	7	4		43	91	92		10	13	11	Unoperated
1	9	5	4	78	155	101	63	8	9	10	9	Biliary cirrhosis—operated
	13	7			202	137			15	13		Unoperated
14	17	21		77	213	127		9	11	10		Unoperated
	15	15	7		160	136			17	18	3	Unoperated
	10	16			216	193	195	14	15	14	15	Unoperated
	18	18	17		189	155	50		15	13	12	Unoperated
6	5	10	13	53	115	84	149	8	9	8	9	Anxiety neurosis
	3	8	3	60	54	151	48		6	13	11	Stones in gallbladder—P. felt normal
4	14	14	14		309	180	94	1	13	9	9	Unoperated
2	12	12	12	53	203	210	172	7	16	16	15	Unoperated
15	8	12	8	160	113	102	112	17	15	15	14	Unoperated
5	15	10	9	53	91	63	61	9	12	13	13	Stricture common bile duct—cicatricial
2	7	8	8	102	176	155	83	15	11	14	14	Hepatitis
5	5	5	5	67	34	80	131	13	11	14	10	Unoperated
6	9	7	5	157	67	103	133	16	11	11	14	Cicatricial stricture common bile duct
6	9	6	7	85	130	99	123	15	15	14	15	Cirrhosis, Laennec

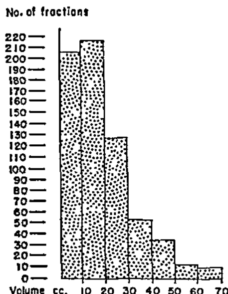


FIG. 3. Frequency distribution of the volumes of 10-minute fractions of pancreatic juice before and after mecholyl injection in nonpancreatic disease.

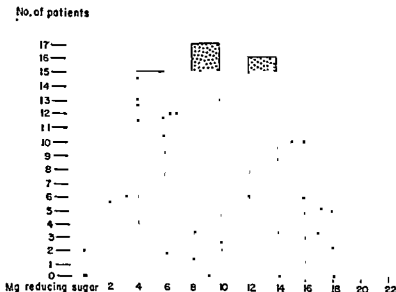


FIG. 4. Frequency distribution of amylase concentration in the pancreatic juice in nonpancreatic disease during 10 minutes after mecholyl injection.

TABLE 4. THE RANGE, MEAN AND MEDIAN VALUES OF THE VOLUMES OF THE FOUR FRACTIONS OF PANCREATIC JUICE IN 169 NONPANCREATIC PATIENTS

FRACTION	RANGE cc.	MEAN VALUE cc.	MEDIAN VALUE cc.
1	1–66	17.4	15.7
2	1–104	20.8	18.5
3	2–58	20.0	16 2
4	1–65	16.0	13.0
		4)74.2	4)63.4
		18.5	15.9

TABLE 5. FERMENT CONCENTRATIONS IN NONPANCREATIC DISEASE

	RANGE	MEAN	MEDIAN
Amylase			
Fraction 1 mg. sugar	1–18	6	4.8
2	2–21	10.4	10.
3	2–21	10.7	10.3
4	3–21	9.3	9.2
Protease			
Fraction 1 mg. nonprot. N	7–285	92	86
2	34–426	188	182
3	14–509	183	161
4	16–584	156	136
Lipase			
Fraction 1 cc. n/10 acid	1–21	10.8	10.7
2	2–25	14.8	14.
3	4–30	14.2	13 4
4	3–20	13.2	12.8

ACUTE PANCREATITIS

During the height of an attack of acute pancreatitis it is obviously undesirable to add the discomfort of the pancreatic function test to the suffering of the patient.

Lagerloef's experience in acute pancreatitis using[6] secretin stimulation points to a rapid return of normal function after subsidence of the acute phase of the disease (see Table 6).

Regeneration after an acute attack may be rapid and complete. In several patients that were explored for acute pancreatitis, the pancreas was enlarged and nodular, but at a subsequent operation, no abnormality was found.

had diabetes. The third attack occurred in July, 1946. He then had epigastric pain and spasm, a serum amylase of 237, and a white count of 17,000.

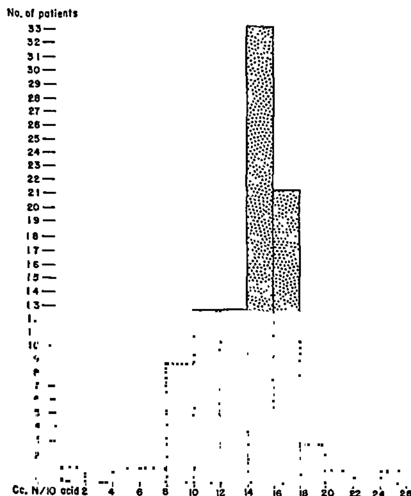


Fig. 6. Frequency distribution of lipase concentration in the pancreatic juice in nonpancreatic disease during 10 minutes after mecholyl injection

In recurrent pancreatitis, enough parenchyma may have been destroyed prior to the last attack to permanently lower function.

In acute pancreatitis, the serum amylase and lipase values are of greater clinical importance than any other laboratory test.

The effect of repeated acute inflammation is seen in the case of J. T., history number 707520, a man of 53. On April 21, 1943, he had sudden epigastric pain, nausea, vomiting, tenderness in the epigastrium, a white

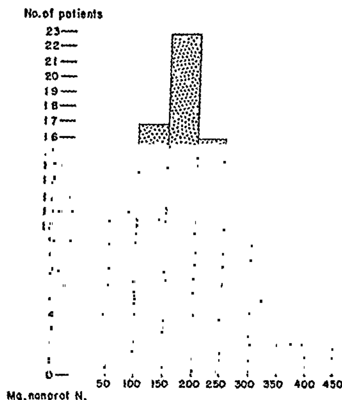


FIG. 5. Frequency distribution of protease concentration in the pancreatic juice in nonpancreatic disease during 10 minutes after mecholyl injection.

blood count of 22,000 and a serum amylase of 244, this is, eight times the normal value. His serum phosphatase was 4, and serum bilirubin only a trace. The cholecystogram showed stones. A cholecystectomy was done. Numerous areas of fat necrosis were seen. The head of the pancreas was indurated. In December, 1943, there was a recurrence of upper abdominal pain, a white count of 18,000 a serum amylase of 288, serum phosphatase of 6.7, and a serum bilirubin of 1.4. He now

The established predisposing causes of acute pancreatitis are gallstones or biliary tract disease and alchohol indulgence. The ease with which radio-opaque material enters the pancreatic ducts when it is injected into the common bile duct suggests the possibility that bile reflux may also be a cause of acute pancreatitis, especially when there is spasm of the sphincter of Oddi.[36, 37, 86]

Chronic Pancreatitis

The results of the pancreatic function test in chronic pancreatitis are listed in Table 7. While the average volume of the fractions was elevated, their *p*H was within normal limits. The concentration of ferments is proportional to the degree of destruction of acinar tissue. Fifteen of the 20 cases (75 per cent) had a diminished ferment concentration. In a series reported by H. Lagerloef[6] after secretin stimulation, 21 of 28 patients had low ferment values. With the same stimulant, Comfort, Gambill, and Bagenstoss[38] reported low values in all of 8 patients with chronic pancreatitis. The combined evidence from three sources indicates that extensive destruction of acinar cells is common in this disease.

It is noteworthy that the juice remains alkaline even in advanced pancreatic disease and that the concentration of each of the three ferments is not uniformly diminished. This irregularity is frequently encountered in pancreatic disease.

Chronic pancreatitis, secondary to obstruction of the duct system by carcinoma of the head of the pancreas, is partly responsible for the diminished function in the latter condition.

The known contributory causes of chronic pancreatitis are similar to those of acute pancreatitis, namely, gallstones and alcoholism. Of 29 cases of chronic relapsing pancreatitis recently reported, 68 per cent used alcohol, and 33 per cent were heavy imbibers.

The calcification so frequently seen in long-standing cases may be a secondary deposition or actual pancreaticolithiasis.[39] About one half of the cases in the present series had calcification. In this condition, the roentgenogram shows clusters of opacities within the confines of the pancreas. This may well be the first intimation of the disease. The components of these pancreatic calculi are calcium and carbonic acid. Normal pancreatic juice contains 138 milli-equivalents of sodium, from 2.2 to 3.2 milli-equivalents of calcium, from 60 to 80 of chlorine, and from 60 to 75 of bicarbonate.[40] It is conceivable that stone formation

TABLE 6. PANCREATIC FUNCTION TESTS IN ACUTE PANCREATITIS, USING SECRETIN
(H. Lagerloef)*

CASE NO.	DAYS AFTER ONSET	BLOOD AMYLASE	VOL. *cc.*	SOD. BICARB. *cc. 0.1 normal*	AMYLASE *units*	PROTEASE *units*	LIPASE *units*	
69	24	29	218	151	42	13	201	
70	0	10						
	5		226	189	222	48	356	
71	9	8.7	299	196	54	63	727	
	15	9.7						
	37		374	348	847	125		
72	2	9.3						
	10	7.7	194	123	98	34	357	
	19		264	227	276	37		first
74	4	4.4	183	122	234	45		attack
	6	7.1						
	13	3 9						second
	20		262	244	939	115		attack
	37		265	252	628	91	2362	
75	0	17.0						
	5		265	257	340	70	835	
	61		278	254	537	73		
77	15	8 1	261	238	597			
78	6		168	129	131			
	42		149	107	342			
79	0	3 0						
	7		282	165	187	65		
	13		196	117	342	56	1300	
Normal Values		**2-4**	**202**	**180**	**634**	**87**	**179**	

*Pancreatic Function and Pancreatic Disease, New York, Macmillan.

The first pancreatic function test taken on Oct. 19, 1943, was normal One of the fractions of the pancreatic juice had a *p*H of 7.6 and normal concentrations of the three ferments. After the third attack (July 24, 1946), the juice was low in lipase. The pancreatic function test done at that time was as follows:

Fraction	*1*	*2*	*3*	*4*
Volume cc	7	5	10	2
*p*H.	7 5	7.5	7.5	7.5
Amylase	3	4	4	4
Protease. . . .	35	74	64	46
Lipase*.	3	4	3	4

*Minimal normal 8 cc

Case II. A colored woman of 25 had from ten to fifteen bowel movements a day and crampy abdominal pains for four months. The stools were large, light yellow, fatty, and at times contained blood. The patient had indulged freely in alcohol. The weight loss was 16 pounds in six months. Physical examination was negative except for generalized tenderness over the abdomen. A roentgenogram showed calcification in the region of the pancreas. The serum amylase was normal. The glucose tolerance test indicated latent diabetes. The pancreatic juice after mecholyl stimulation was alkaline but contained only traces of ferments.

PANCREATIC FUNCTION TEST

Fraction	*2*	*3*	*4*
*p*H	7.5	7.6	7.7
Volume cc.	15.	12.	9.
Amylase	0.8	2.8	1.
Protease	low	low	low
Lipase	very low	very low	very low

The pancreas was completely removed; it was hard and nodular and contained numerous calculi, some of which blocked the duct. The stones were pure white and on analysis were found to be almost pure calcium carbonate. Microscopically, the organ showed complete replacement of parenchyma by fibrous tissue. After the pancreatectomy, 75 per cent of ingested fat was absorbed; this was increased to 81 per cent when five panteric pills were taken with each meal. The diabetes was controlled on a diet of 300 grams of carbohydrate, 70 of protein, and 75 of fat, by 60 units of globin insulin. Later, the insulin was reduced to 30 units without glycosuria and with blood sugars of 194 and 112.

Repeated attacks of acute inflammation may eventually destroy sufficient acinar tissue to lower the ferment concentration in the pancreatic juice.

Case III. A man, aged 54, had severe epigastric pain and vomiting in June, 1944. His abdomen was boardlike and exquisitely tender in the epigastrium. White blood count was 28,000. Serum amylase was markedly elevated. Fever and symptoms persisted, and a mass developed in the upper abdomen. Drainage liberated 1,000 cc. of purulent fluid containing flecks of necrotic fat. He recovered and was discharged in September, 1944.

in the duct is primary in certain patients. Nothmann[41] has recently found a considerable phosphatase content in the pancreatic juice of dogs, and a rise in serum phosphatase after ligation of the pancreatic duct. The average phosphatase of the serum of dogs (Bodansky units) is 2 before and 13.8 from four to ten days after the operation. He also observed an elevated serum phosphatase in two patients with steatorrhea and other evidence of chronic pancreatitis.

The presenting symptom of chronic pancreatitis may be epigastric pain, persistent or intermittent diarrhea, large fatty stools, weight loss, or jaundice. As the islands of Langerhans resist the inflammatory process longer than the acini, diabetes is usually a late symptom and is indicative of widespread destruction.

The following cases are illustrative.

Case I. The first symptom of this woman of 46 was bulky stools, and this was followed by epigastric pain. The roentgenogram showed calcified areas in the pancreas. Exploratory operation at another hospital revealed the presence of sacs of sand in the pancreas.

The pancreatic secretion was almost devoid of ferments.

PANCREATIC FUNCTION TEST

Fraction	*10 min.*	*20 min.*	*30 min. p. mecholyl*
Volume cc.	17	16	22
pH	7.2	7.9	6.7
Amylase	0	0.1	0.1
Protease	low	low	low
Lipase	very low	very low	very low

The serum amylase of 32 was high, considering the minimal amylase values in the pancreatic juice. The lipase was inadequate for normal fat digestion. Of 103 grams of fat consumed in a three-day period, 64 grams were recovered in the stool. A complete pancreatectomy was done. The pancreas measured 16 cm. by 4.5 cm. On section, the ducts were blocked by white calcareous material resembling coral. The dilated duct of Wirsung was surrounded by dense connective tissue.

Cross section showed a number of small, round openings surrounded by dense fibrous tissue. Microscopically, no normal tissue was seen. The calculus contained 38.2 per cent of calcium. The theoretical amount for calcium carbonate is 40 per cent. The pathologist concluded that the fibrosis was secondary to the duct occlusion.

In spite of the many episodes of inflammation and objective evidence of pancreatitis, the pancreatic function test was normal indicating regression or regeneration.

Roentgenogram of the upper abdomen at this time showed no calcification.

At the last operation, in January, 1947, the main body of the pancreas was soft and normal. The terminal 3 or 4 cm. of the tail felt lumpy and was resected. It showed fibrosis microscopically.

The diagnostic value of the pancreatic function test is well illustrated in cases V and VI.

Case V. A man of 50 had six weeks of epigastric pain unrelieved by food. The pain was also felt in the back and in both upper quadrants. Aside from a blood pressure of 280/180, physical examination and roentgen examination of the gastro-intestinal tract, including the colon, were negative. Serum phosphatase and bilirubin were normal. The electrocardiogram showed myocardial damage. The glucose tolerance test indicated mild diabetes. The amylase concentration was below the normal minimal value of 4.

Pancreatic Function Test

Fractions	*1*	*2*	*3*	*4*
Volume cc. ...	15	9	20	40
*p*H..	7.2	7 0	7.3	6.8
Amylase	0.7	2 0	2 0	2.0
Protease	60.0	22.0	13 0	21.0
Lipase	8 0	13.0	12.0	9 0

At exploration, the surgeon felt only questionable thickening of the head of the pancreas. The pain continued after operation. The patient died one month later of cerebral hemorrhage. At autopsy, the body and tail of the pancreas were unusually firm, and the head appeared to be a fibrotic collar about the duct of Wirsung, averaging about 4 mm. in thickness. About 2 cm. distal to the duodenum, all that remained was a cystic mass about 1.5 cm. in diameter. Its walls were hemorrhagic, and it was filled with chalky, cheesy material. Small areas of fat necrosis were seen in the serosal fat over the pancreas. Death was due to hemorrhage involving the right caudate nucleus, internal capsule and putamen. The difficulty of diagnosing disease of the pancreas by surgical exploration is repeatedly mentioned in the literature.

In January, 1945, he suffered an attack of right upper quadrant pain with localized tenderness and spasm. An enlarged gallbladder with stones was removed.

In November, 1946, he had another attack of acute pain associated with a mass in the upper abdomen. A pancreatic cyst was drained. The fluid measured 750 cc. and contained the three pancreatic ferments. During convalescence, a pancreatic function test gave the following results:

Fraction	1	2	3	4
*p*H	8.5	7.1	7.0	7.0
Amylase	2.9	2.1	0.4	0.3
Protease	21.0	81.0	37.0	7.0
Lipase	8.0	8 0	6.0	6 0
Volume	35	24	24	21

COMMENT. Minimal normal values—amylase 4, protease 50, lipase 8.

The recuperative power of the pancreas is illustrated in another case.

Case IV. M. G., aged 38, was first seen in February, 1938. He had had moderate epigastric distress for several years which had recently increased. White blood count was 22,000. During the next month he had fever and jaundice. Serum bilirubin was 5.3 and serum amylase 73 (normal 30). At operation, the gallbladder and common bile duct contained stones: The head of the pancreas was enlarged and firm. Though cholecystectomy and choledochotomy were done, episodes of a similar nature recurred. In November, 1940, he was re-explored. At this time there were no stones in the common duct, but the head of the pancreas was hard, and the lower end of the common duct was narrowed. In January, 1942, a division of this stricture of the papilla was done. After several lesser attacks, a severe, acute seizure occurred in November, 1946.

PANCREATIC FUNCTION TEST

Fraction	1	2	3	4
Reaction	Acid	Alkaline	Alkaline	Alkaline
Amylase		11	11	11
Protease		223	233	81
Lipase		17	17	14

1	18	21	6	ac	7.9	7.8	7.1	—	+	1.	+	—	+	+	+	3.5	13	8	10	Calcification and cyst formation. Normal P. F.T.
8	15	4	1	6.	7.0	7.8	7.0	1.	+	I	qns	+	1.	1.	qns.	4.	7	7	3	Fibrosis and calcification—later diabetes
	15	12	9	—	7.5	7 6	7.7	—	0 8	2.8	1.	—	0	0	0	—	0.4	0.5	0.5	Stones in P. duct, fibrosis and cystic degeneration. Complete pancreatectomy
Ac.	16.5	16	22	Ac	7.2	7.9	6.7	0	0	0.1	0.1	—	1.	1.	1.	—	0.9	1.4	2.1	Calcification. Fat absorption ca. 38%
16	9	20	40	7.2	7.3	7.3	6 8	0 7	2 0	2 0	2.2	60	22	13	21	8.7	12.8	12.3	9.4	Diab. G.T.T. Autopsy. Fibrosis and cyst formation
13	41	21	3.2	7 3	7 3	7.3	7 5	0 7	0 1	0 3	1 5	10	7	7	1.4	2.3	1.4	2 3	1.7	{Calcification and cyst formation. Diabetes—
6 5	4 8	98	5	7.5	7.5	7 5	7.5	0.7	2 0	0 7	6	19	2	7	6	5 6	1.4	2.0	3.5	{S A. 81
25	25	79	54	8 3	8 1	7 9	8 4	+	+	+	+	+	+	+	+	2 0	2 0	2.0	1 0	Relapsing Pctis. 3 operations. False cyst. P. hard & thick. Diab. G.T.T.
60	30	3	5	ac.	7.0	7.0	6 9	0 3	0.4	1.1	0.4	4.8	5.9	3 9	8.9	0 5	0 5	0.6	0 6	Calcification. Partial pancreatectomy
4	30	24	28	7 0	7.0	7.4	7 2	3 2	11.6	15 6	12 6	36	100	46	117	6.0	12.	5.0	13	Calcified P. Cyst of body of P. Autopsy — Chr. Pctis with some normal tissue in head of P.
Ac.	68	16	10		7 5	7.5	7.0	—	10.3	1 7	18	—	7.	35	32	—	0 6	4.2	2.5	Calcification. Alcoholic
36	59	35	65	7.5	7.5	7 5	7 0	10.7	10.7	10 7	10.7	75	72	43	36	14	12	12	13	Gallstones. P. large and firm. Stones in ampulla C.B.D.
6	11	47	13	7 5	7.3	7.1	7.1	13	1	.03	13	5	6	11	10	1.	0.95	1.	1.	Unoperated. Had acute attack followed by calcification of P.

Table 7. Pancreatic Juice in Operated Cases of Chronic Pancreatitis

Volume cc. Fractions				pH Fractions				Amylase Concentration Fractions				Protease Concentration Fractions				Lipase Concentration Fractions				Diagnosis and Remarks
1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
40	33	8	5	6.8	8.	8.	8.	low	+	+	+	+	+	+	+	0.7	3	1.6	0	Stones in G.B. and C.B.D. Biopsy showed patchy thickening in the head of P. Low lipase. Chr. Pctis.
	36	26	10		7.	8.	8.						+	+	+	0.4	0 5	0.5		
40	36	56	53	7 2	7.5	7 3	ac.	0	0	0	0	0	0	0	0	2.	10.	4	9	Resection hd. and body of P. which showed calcification
40	26	25	15	7.5	7.5	7.5	7.5	0	0	0	0	0	0	0	0	21	28	22	21	Diab. G.T.T.—S A. 49. Pancreaticoduodenectomy. P. duct contained numerous calculi. Extensive fibrosis of P.
34	34	44	36	7.5	7.5	7.5	7.5	0	+	+	+	0	+	0	0	2	10	2	0	Nodular body and tail P. histol.—fibrosis
5.5	14.5	6	9	7.5	7 5	7 5	ac	0	0	0	–	l.	l.	l.	–	0.8	0 6	0.7	5.5	J.—diab —Palpable G.B.
11	15	7	1	7 5	7 5	7.5	7.5	l.	l.	l.	0	0	0	0	0	6.	11.	4.	0	J.—S.A. 70. At operation P. large and hard
26	41	30	4	ac.	7.5	7.5	7.5	l.	+	+	+	l.	l.	l.	+	5	3	0.2	0.3	Stones in G.B. Hd. P. thickened. Diab. G.T.T. Normal P.F.T. Obstructive J. S. A. 237. Numerous hard areas in P.

common bile duct reported by Walters[43] were due to chronic pancreatitis, yet recently Peterson and Cole[44] described three and Bisgard[45] two such cases in which the common bile duct was stenosed by inflammatory tissue in the pancreas.

Cancer of the Pancreas

Surgical exploration does not always furnish the exact diagnosis in suspected cases of carcinoma of the pancreas. The value of a diagnostic exploration depends largely on the experience of the surgeon. Palpation of the organ may be misleading because the normal pancreas varies in size and consistency. As we shall see, even a biopsy may be deceptive; because of the danger involved, it is at best a questionable procedure. The operator may be unable to distinguish between a primary tumor of the head of the pancreas and one that arises in the duodenum or ampulla and invades the adjoining organ. If metastases are obvious, the surgeon may decide to close the abdomen without further investigation, or if the growth is extensive, it may be impossible to determine its primary site. In the 22 cases of verified carcinoma of the head of the pancreas, the pancreatic juice was abnormal in 20 (90 per cent). (See Table 8.)

In exceptional cases, the pancreatic juice may be normal when the organ is extensively diseased, if a modicum of uninvolved tissue remains. This may be the case in tumors arising in the body and extending to the right. A tumor of the lower part of the head may grow downward without involving either duct. Eusterman and Wilbur[46] speak of 11 cases of carcinoma of the head without jaundice. An interesting and instructive discussion of the clinical and laboratory features of carcinoma of the pancreas is given by Pratt.[47]

Patient P. R., aged 58, had upper abdominal pain, jaundice, an enlarged liver, moderate anemia and clay-colored stools. The pancreatic function test was normal. The first two fractions were acid.

Pancreatic Function Test

Fractions	*3*	*4*
Volume cc.	11	6
pH.	7.5	7.5
Amylase	Normal	Normal
Protease	High	High
Lipase cc. 0.1 N acid	12.0	10.0

Case VI was a woman of 50 who was admitted in Feb., 1944. For 2 months she had complained of pain in the right gluteal region, right lower and upper quadrants with vomiting and fever. Elevation of the right diaphragm and a pushing down of the right kidney by a mass was noted. Tenderness was maximum in the upper midabdomen. White blood count was 15,000, with 64 per cent polynuclear cells. The serum amylase was normal. Roentgen examination of the gastro-intestinal tract showed that the antrum and pylorus were displaced upward, and that there was a widening of the duodenal loop suggesting a mass in the head of the pancreas. Blood chemistry was normal. The diagnosis of acute pancreatitis with abscess or pancreatic cyst was favored. The pancreatic function test was normal.

	Pancreatic Function Test			
Fractions	*1*	*2*	*3*	*4*
Volumes cc.	10	18	15	9
*p*H	8.1	7.9	8.0	8.3
Amylase	7.0	10 0	9.0	17.0
Protease	Normal	Normal	Normal	Normal
Lipase	12.0	18.0	18.0	17.0

Minimal normal values—amylase 4, protease 50, and lipase 8.

At operation, the pancreas was pushed forward by a mass the size of a grapefruit *which was attached to the posterior* abdominal wall. Biopsy revealed lymphosarcoma.

Complete destruction of the pancreas by fibrosis and calcification may occur without pain. Pasternak[42] reports the case of a man of 57 with intractable diarrhea, emaciation, diabetes, and calcification without pain, demonstrated by roentgenogram. At autopsy, the gallbladder was distended with white bile, but the bile ducts were normal and patent. The pancreas weighed about five times the normal, due to stones and sand. Many cysts were present.

His second case was a man of 46 with active pulmonary tuberculosis and diabetes. He had no abdominal symptoms or diarrhea. Postmortem showed bilateral tuberculosis of the lungs and a pancreas weighing 180 grams, that is, more than twice the normal. The latter was hard and gritty. The ducts were filled with calculi. Histologic examination showed extensive fibrosis and cyst formation.

Jaundice due to stenosis of the common bile duct by chronic pancreatitis is a rare condition. None of the eighty cases of stenosis of the

Pancreatic Function Test					
Fractions	*1*	*2*	*3*	*4*	*Normal Minimum*
Volume cc.........	10	20	14	11	
pH................	7.0	7.0	7.0	7.0	
Amylase...........	0.03	1.2	0 01	0.7	4.0
Protease...........	28.0	36.0	29 0	34.0	50.0
Lipase.............	6.0	7.0	7.0	7.0	8.0

glandular by fibrous tissue. There was no evidence of carcinoma. She was readmitted in April, 1946, for continuous epigastric pain and tenderness. The serum phosphatase was 14, serum bilirubin negative, cholesterol 199, and serum amylase 32. Exploration revealed metastases in the omentum and elsewhere and a large amount of fluid in the peritoneal cavity. At autopsy, the head of the pancreas was the seat of an undifferentiated carcinoma which had spread to the regional lymph nodes, liver and peritoneum. Bile and pancreatic ducts were obstructed. The body and tail of the pancreas showed atrophy and mild chronic inflammatory changes

In the next patient, carcinoma may have been superimposed on chronic pancreatitis. R. S., aged 50, complained of fullness after meals. Roentgen examination of the gastro-intestinal tract was negative. The gallbladder showed poor concentration. At exploration in another city in the latter part of 1942, the gallbladder was thickened, and the head of the pancreas was enlarged and edematous but not hard. The gallbladder was anastomosed to the duodenum in the assumption that the patient had a chronic pancreatitis. He entered the Presbyterian Hospital two and a half years later. He had no jaundice and a normal serum phosphatase. The pancreatic function test was normal.

Pancreatic Function Test				
Fraction	*1*	2	*3*	*4*
Volume	6	6	4.5	3 0
pH...	8 2	8 5	8 6	8 2
Amylase	10 0	13 0	13.0	13 0
Protease. . . .	77 0	95 0	389 0	81 0
Lipase...	13 0	14 0	14 0	12.0

Attacks of upper abdominal pain, mild fever and leukocytosis persisted. In February, 1946, he had a diabetic glucose tolerance test. Stools contained large amounts of neutral fat. He reentered the Presby-

A partial pancreatectomy was done. The growth in the head involved the common bile duct but not the pancreatic duct. Here, as elsewhere, the unusual location or spread of a cancer may increase the difficulty of diagnosis.

There is a possibility that carcinoma may arise in a chronically inflamed or fibrotic pancreas, as it does in a cirrhotic liver. For example, H. K. was admitted in May, 1945, for nine years of periodic midabdominal colicky pain increasing in severity and radiating to the left upper quadrant and back. The pancreatic juice was low in amylase only. In August, 1945, the pain had extended to the lower abdomen, low back, and right upper quadrant. There was tenderness in the epigastrium. *At operation, the body and tail were infiltrated by cancer,* as well as the posterior abdominal wall. A metastatic mass in the omentum showed carcinoma.

Brocq and Miginiac[48] *refer to a case of carcinoma of the head,* secondary to severe chronic pancreatitis. Presumably the fibrosis had destroyed the islets and produced diabetes before the development of *the cancer. These authors maintain that the differentiation of carcinoma of the head from chronic pancreatitis is at times impossible, despite* biopsy and other diagnostic procedures. This conclusion is supported *by experience in this and other institutions.*

The fibrosis commonly associated with carcinoma of the head of the pancreas may completely conceal the growth and thus deceive the surgeon. *The diagnosis of cancer may be well established on clinical* and laboratory grounds. At exploration, the entire organ is uniformly hard, and the frozen section shows only fibrosis. A short-circuiting operation relieves the jaundice, and the patient may regain full health for a remarkably long period. Indeed, several years may elapse before the progression of the malignant process becomes apparent.

Mrs. B. belongs in this category. In April, 1945, she developed pain in the epigastrium radiating to the costal margins and back. Colon and gastro-intestinal roentgenograms were negative, as was a special study of the small intestines. She had achlorhydria, a diabetic glucose tolerance curve and an elevated serum amylase on two occasions (50 and 61). (Normal maximum = 30.) The pancreatic function test was definitely abnormal.

At operation on December 3, 1945, the entire pancreas was hard and contracted, and the common bile duct enlarged to about 1 cm. A cholecystenterostomy was done. Biopsy showed a replacement of

Fraction	Pancreatic Function Test 1	2	3	4
Volume cc.	4	4	22	8
*p*H.	7	7.2	7.6	8
Amylase	0 5	0.6	0.5	0.9
Protease	qns.	low	low	low normal
Lipase	very low	very low	very low	very low

The pancreatic function test showed almost complete absence of ferments though the *p*H of the fractions varied between 7 and 8. At operation, the head felt hard and nodular, but the body and tail were also hard and cystic. A radical pancreaticoduodenectomy was done. The specimen showed no obstruction of the pancreatic duct. The common bile duct showed soft swelling of its wall but could be probed down to the papilla of Vater without meeting an obstacle. Histologically, the pancreas showed much fibrosis with cystic dilation of some of the pancreatic ducts. There was no evidence of malignancy. After operation, on a known fat intake he absorbed 89 per cent of the ingested fat. Mild diabetes was present. In August, 1946, he was admitted for recurrent pyrexia and diabetes. Diarrhea and hematemesis developed later. Serum amylase was 25, phosphatase 50, and serum bilirubin 1.7. On careful review of the sections of November, 1944, *adenocarinoma was discovered. At the autopsy, in January, 1947,* carcinoma in different parts of the upper abdomen was found.

In cancer of the body of the pancreas, there is usually enough uninvolved tissue to the right of the lesion to provide normal pancreatic juice. The close proximity of the body to the celiac plexus accounts for the frequency of epigastric and back pain in carcinoma of the body in contrast to carcinoma of the head, where obstructive jaundice is the usual presenting symptom. In 99 of 113 cases of carcinoma of the head reported by Walters and Dehne,[49] painless jaundice was the initial symptom. Cattell[50] had a similar experience in 14 of the 15 patients with carcinoma of the head of the pancreas. Grauer,[51] on the other hand, found that epigastric pain was an early symptom in 20 of 34 autopsied cases According to Berk,[52] pain occurs more frequently and earlier than jaundice.

Of the 6 tabulated cases of *carcinoma of the body,* 5 had normal pancreatic juice. The difficulty in the diagnosis of carcinoma of the body is well exemplified by the case on page 34.

terian Hospital in April, 1946, for epigastric pain and fever. The second pancreatic function test (April 11, 1946) was abnormal. Fractions 1 and 2 were acid.

PANCREATIC FUNCTION TEST

Fraction	*3*	*4*
Volume	11	4
*p*H	7.3	7.3
Amylase	7.0	7.0
Protease	42.0	45.0
Lipase	4.0	4.0

Roentgen examination showed no enlargement of the duodenal loop but metastases in the lungs. At operation, metastases in the liver and infiltrating carcinoma of the head of the pancreas were found. Was this a slow-growing tumor from the outset, or was it a cancer superimposed on chronic pancreatitis?

Even a biopsy from the head of the pancreas may not disclose the underlying pathology. G. B., a woman aged 56, was admitted in August, 1943, for ten days of painless jaundice with an enlarged gallbladder and chemical evidence of obstructive jaundice. Roentgen examination of the gastro-intestinal tract was negative. The pancreatic *juice had an abnormally low lipase concentration, indicating malfunction.* The serum amylase was slightly elevated.

At operation, the gallbladder and common duct were distended. The entire pancreas felt hard, like carcinoma, but a biopsy from the head of the pancreas showed only fibrosis. A cholecystenterostomy was done. She was readmitted in December, 1944, for pain in the upper abdomen and a mass in this location. She now had diabetes. The serum phosphatase was 10.7, and roentgen examination showed a narrowing of the second part of the duodenum. The second operation revealed metastases in the liver.

The predominance of fibrous tissue may interfere with accurate histologic diagnosis even in the pancreatectomy specimen. The following case is most instructive.

L. C., aged 60, was admitted in November, 1944, for painless obstructive jaundice. Roentgen examination of the stomach and duodenum was negative. The liver was palpable two fingers below the costal margin.

6	6	4 5	3	8 2	8.5	8 6	8.2	9 7	13.3	13 3	13.3	77	195	389	81	13.	14.	14.	12.	Ca head of P.
15	4	6	5	5 6	7.2	8 2	8.5	6	7	1.2	1.9	10	15	10	31	l.	1.5	1.4	3.3	Ca. head of P. with secondary fibrosis
6	31	33	20	5 4	7.1	7.1	7.1	ac.	.04	.04	.04	ac.	6	3	19	ac.	0.5	0.7	0.7	Ca. head of P.
14	4	7	2	7.8	7 0	7.8	7 0	8.3	6.	17	17	43	36	76	98	3 4	3.5	3.0	2.5	Ca. head of P.
2	6	11	29	ac.	7 5	7.5	7 5	0	+	+	l.	qns.	l.	l.	l.	qns.	16 8	17.6	l.	Ca. head of P.
1	11	8.5	4 5	7 5	7.5	7.5	7.5	l.	+	+	+	+	+	+	+	—	7.4	4.	2.	Metastatic Ca. involving P.
ac	ac.	3.	10	—	—	7.2	7 1	—	—	+	+	—	—	159	139	—	—	17.5	14.6	Ca. body of P. with metastases
ac	28	ac	12	—	6.7	ac.	7 1	—	2 5	—	1 9	—	41	—	43	—	14	—	12	Ca. P.
7.5	8.5	17	5	8.	7 8	7.5	7.5	2.1	1.3	5 9	15	+	+	+	+	9.5	12.6	16.4	16 8	Ca. body of P.
—	—	8	3	—	—	7 9	8 2	—	—	5.3	5.1	—	—	91	95	—	—	11.7	13.	Ca. body of P.
47	7	6.	41	7 5	7.5	7.5	7.5	2 9	6 1	4 5	2.3	48	92	129	55	7.3	7.0	10.	8.4	Ca. body of P.
5.5	6.5	3	3	7 2	7 2	7 2	7.2	5.	8.6	7.6	4 1	21	45	42	24	1.3	2.9	6.3	3.5	Ca. P. entire autopsy
2	0	5	2	7.4	0	7.9	7.9	3 8	—	10 6	11.3	7.	0	107	47	0.5	—	4.7	2 2	Ca. body of P. with extension into head. Autopsy
6.5	8.5	12	7	7.2	7.2	7.2	7.2	1 8	2 2	3 6	3 3	2.	6	3	7	0.7	0.8	0.8	0.8	Ca. stomach metastases to P.
ac.	17	11	15	ac	7 3	7 4	7 0	—	0 1	.003	0 4	—	9.4	12.	10.	—	1.1	1.1	.9	Ca. head of P.
13	6	34	15	7 2	7 4	7.4	7.3	6.2	8 0	5.9	7.4	46	92	120	95	13	14	12	12	Ca. head of P.
26	14	14	3	6 8	7 5	7 5	7 5	0 2	0 6	0 5	0 2	1.4	1.6	1.4	1.2	0.4	0.4	0.4	0.4	Ca. head of P.
22	25	45	27	7 5	7 5	7.5	7.5	0.9	1.2	0 1	0.1	7	12	6	6	0.8	0.9	0.4	0.4	Ca. head of P.
13	7	8	14	7.0	7.1	7 3	7 3	10	6	10	15	90	98	120	146	7.	5.0	8	14	Ca. body and tail of P.
18	9	27	57	8 5	7.7	7 1	ac.	3	4.6	5.6	—	36	62	81	—	11.	13	14.	—	Ca. head of P.
15	5	7	ac	7.2	7 5	7 5	ac	2.7	1.0	0 9	—	33	41	36	—	Not done				Ca. head of P.

Abbreviations
P. = Pancreas
Ca = Cancer
C.B. = Common bile
P.D = Pancreatic duct
l. = low

Minimum Normal Values: Amylase 4
Protease 50
Lipase 8

TABLE 8. PANCREATIC JUICE IN OPERATED CASES OF CARCINOMA OF THE PANCREAS

Volume cc. Fractions				pH Fractions				Amylase Concentration Fractions				Protease Concentration Fractions				Lipase Concentration Fractions				Diagnosis and Remarks
1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
18	9	11	6	ac.	7.5	7.5	7.5	0	0	+	+	0	0	+	+	0	0	12.	10	Ca. head of P. obstructing C.B. but not P.D.
11	18	36	25	ac.	7.5	7.5	7.5	0	+	+	0	0	0	+	1.	2.	5.	9.	5.	Ca. head of P.
16	24	24	27	ac.	7.5	7.5	4.5	ac.	1.	1.	ac.	−	0	0	−	−	3.	2.8	−	Ca. head of P. marked fibrosis
26	16	13	13	7.5	7.5	7.5	7.5	0	0	0	0	+	+	+	+	3.	9.	6.	9.	Ca. head of P. no jaundice
7	5	17	7	ac.	7.5	7.5	ac	ac.	+	+	ac.	1.	1.	1.	1.	10 6	7.	7.4	ac.	Ca. head of P.—Autopsy
3	4	5	1	7.5	7.5	7.5	7.5	+	+	+	+	1.	1.	+	0	0	1.	1.8	−	Ca. head of P.—Autopsy
15	6	6	5	7.5	7.5	7.5	7.5	0	0	0	0	0	0	0	0	0 7	0.7	0.7	0.8	Ca. head of P.—Autopsy
7	9	5	10	7.5	7.5	7.5	7.5	+	+	+	+	+	+	+	+	0.2	1.0	4.0	4.0	Ca. head of P.
16	2	36	−	8.0	7.0	7.3	ac.	1.	+	+	−	1.	1.	+	−	0.2	0	−	−	Ca. head of P. jaundiced
7	4	4.5	8	ac.	ac.	7.6	7.4	−	−	+	+	−	−	+	+	−	−	3.8	3.3	Ca. head of P. Autopsy
ac.	ac.	7.	15	ac.	ac.	7.3	7.5	−	−	+	+	−	−	1.	1.	−	−	0.4	0.5	Ca. head of P.
−	3	6	−	−	7.4	7.9	−	−	−	+	+	−	−	1.	1.	−	−	2.8	5.6	Ca. head of P.
−	12.5	13	4	−	7.2	7.0	7.6	−	+	+	+	−	0	0	0	−	2.6	1.8	−	Ca. head of P.
10	20	14	11	7.0	7.0	7.0	7.0	.03	1.2	1	67	28	36	29	34	5.7	5.8	7.3	6.8	Ca. head, body and tail of P. Atrophy and fibrosis
8.5	4.	12	7.5	6.6	7.9	7.8	7.9	2.1	.7	.6	1.7	4	5	4	3	1.7	1.6	.7	1.7	Ca. head of P.
13	12	7.	47	6.9	7.3	8.1	7.2	2.7	4.1	16.7	16.7	35.3	44	181	37	3.5	2.9	2.5	2.5	Ca. head and body of P.
6	5	4.5	20	7.3	7.3	7.3	7.3	7.8	8.1	10.6	9.1	103	101	167	79	7.1	6.3	7.5	5.0	Ca. head of P.

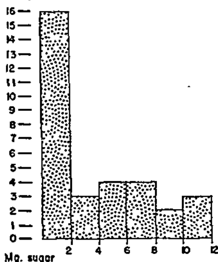


Fig. 7. Frequency distribution of amylase concentration in the pancreatic juice during 10 minutes after mecholyl injection in proved cases of carcinoma of the head of the pancreas and chronic pancreatitis.

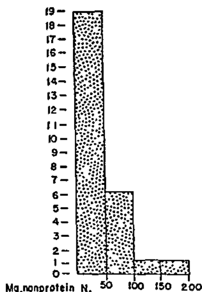


Fig. 8. Frequency distribution of protease concentration in the pancreatic juice during 10 minutes after mecholyl injection in proved cases of carcinoma of the head of the pancreas and chronic pancreatitis.

A. A., aged 56, was admitted in December, 1941, for ten weeks of generalized abdominal pain. The pain was most intense in the back, right lower, and left upper quadrants of the abdomen and was associated with anorexia, nausea and diarrhea. Roentgen examinations of the alimentary tract, intravenous pyelogram, serum amylase and pancreatic function test were normal. Two fractions of alkaline juice were obtained with high concentrations of amylase, protease and lipase. Exploration revealed a thickened cecum. All other organs, including the pancreas, seemed to be normal. Pain persisted after the operation. After visiting various clinics, it was concluded that he was suffering from a psychosomatic or an allergic disorder. His symptoms continued, and in June, 1942, a mass was palpable in the right lower quadrant. He died in July, 1942. At the autopsy, an adenocarcinoma of the body and tail of the pancreas was found. The growth had invaded the abdominal wall, peritoneum, lymph nodes, mesentery, left adrenal, and retroperitoneal tissues.

The second case was a man of 68, a coal miner with diffuse lower abdominal pain, who was admitted in July, 1945. He had lost 36 pounds and had recently developed diabetes. Roentgen examination of the alimentary canal was negative. Serum amylase was 21. In the pancreatic function test, only the third and fourth fractions were obtained.

PANCREATIC FUNCTION TEST

Fractions	3	4
Volume cc.	8	3
*p*H	7.9	8.2
Amylase	5.3	5.1
Protease	low normal	low normal
Lipase	low normal	low normal

The concentrations of the ferments were on the low side of normal. At operation, the body of the pancreas was replaced by tumor, but the head was not completely involved. Biopsy of a nodule in the omentum showed carcinoma.

The concentration of ferments in the combined series of proven cases of chronic pancreatitis and carcinoma of the head of the pancreas has been graphed in Figures 7, 8 and 9. The difference in the frequency distribution of ferment values in nonpancreatic and pancreatic disease is obvious from a comparison with Figures 4, 5 and 6.

suggests an ampullary lesion, as does intermittent jaundice. Roentgen examination of the duodenum may be helpful, but on the whole the symptoms and signs of the two conditions are similar. The pancreatic function test provides the best means of differentiation. In 18 operated cases of carcinoma of the bile ducts, the pancreatic juice was normal in 15 (83 per cent) whereas in carcinoma of the head of the pancreas it was normal in 10 per cent.

Andrus and associates[14] report two cases of obstructive jaundice with normal pancreatic juice. The one had a carcinoma of the bile duct proximal to the ampulla, the other had a carcinoma of the duodenum completely obstructing the opening of the ampulla but with a large accessory pancreatic duct 5 cm. proximal to it.

In carcinoma of the papilla of Vater, the results of the pancreatic function test depend on the patency and anatomy of the ducts. In three of four normal people, both ducts are patent. The unusual result in patient 686471 was due to an anatomic anomaly. A man of 56 had upper abdominal pain, vomiting, an enlarged liver, and jaundice. Serum phosphatase was 71, and serum bilirubin was 9 mg. The ferment concentration in the pancreatic juice was normal.

Fractions	*1*	*2*	*3*	*4*
Volume cc.	11	20	10	2.5
*p*H	7.5	7.5	7 5	7 5
Amylase conc.	high	high	high	high
Protease conc.	normal	normal	normal	normal
Lipase	10 0	14	15	12

The pancreatic juice contained blood.

At operation the gallbladder was markedly distended and did not empty on pressure. The common duct was wide, measuring from 2 to 3 cm. in diameter. Its contents could not be expressed through the ampulla. The head of the pancreas did not feel indurated, but a definite nodule was felt in the region of the ampulla. The surgeon thought the findings were conflicting. Normal pancreatic juice had been obtained, yet the opening of the ampulla was obstructed. A resection of the head of the pancreas, duodenum, and antrum of the stomach was done.

In the specimen, the pancreatic duct ended in a duodenal papilla about 2 cm. proximal to the ampulla without an apparent opening.

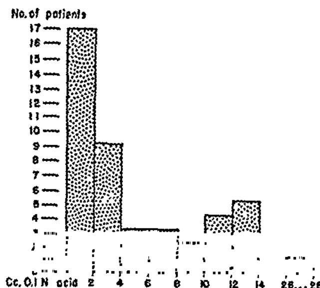


FIG. 9. Frequency distribution of lipase concentration in the pancreatic juice during 10 minutes after mecholyl injection in proved cases of carcinoma of the head of the pancreas and chronic pancreatitis.

At the Presbyterian Hospital, *most of the cases of carcinoma* of the pancreas are found to be inoperable. Patients with vague upper abdominal symptoms (such as anorexia, epigastric or lumbar pain) and weight loss should be explored if the usual diagnostic measures are negative. Only thus is there a possibility that partial or complete pancreatectomy may become a life-saving procedure.

CARCINOMA OF THE BILE DUCTS

In Ransom's[53] series of 109 cases of verified tumors of the pancreas or extrahepatic bile ducts, 49 involved the head of the pancreas, and 26 the bile ducts. The operative diagnosis was not always confirmed at necropsy. In 10 operated cases, 6 were thought to involve the pancreas and 3 the bile ducts, but at necropsy it was found that 7 originated in the ducts and only 3 in the pancreas. In a study of necropsy material at a large urban hospital, Shapiro and Lifdendahl[54] found that *carcinoma of the bile ducts was three times as frequent as carcinoma* of the pancreas. There is obviously a disparity between clinical and pathologic experience.

Heretofore, it has been difficult or impossible to distinguish between the two conditions. The presence of blood in the duodenal secretion

suggests an ampullary lesion, as does intermittent jaundice. Roentgen examination of the duodenum may be helpful, but on the whole the symptoms and signs of the two conditions are similar. The pancreatic function test provides the best means of differentiation. In 18 operated cases of carcinoma of the bile ducts, the pancreatic juice was normal in 15 (83 per cent) whereas in carcinoma of the head of the pancreas it was normal in 10 per cent.

Andrus and associates[14] report two cases of obstructive jaundice with normal pancreatic juice. The one had a carcinoma of the bile duct proximal to the ampulla, the other had a carcinoma of the duodenum completely obstructing the opening of the ampulla but with a large accessory pancreatic duct 5 cm. proximal to it.

In carcinoma of the papilla of Vater, the results of the pancreatic function test depend on the patency and anatomy of the ducts. In three of four normal people, both ducts are patent. The unusual result in patient 686471 was due to an anatomic anomaly. A man of 56 had upper abdominal pain, vomiting, an enlarged liver, and jaundice. Serum phosphatase was 71, and serum bilirubin was 9 mg. The ferment concentration in the pancreatic juice was normal.

Fractions	*1*	*2*	*3*	*4*
Volume cc.	11	20	10	2.5
*p*H	7.5	7 5	7.5	7.5
Amylase conc.	high	high	high	high
Protease conc.	normal	normal	normal	normal
Lipase	10 0	14	15	12

The pancreatic juice contained blood.

At operation the gallbladder was markedly distended and did not empty on pressure. The common duct was wide, measuring from 2 to 3 cm. in diameter. Its contents could not be expressed through the ampulla. The head of the pancreas did not feel indurated, but a definite nodule was felt in the region of the ampulla. The surgeon thought the findings were conflicting. Normal pancreatic juice had been obtained, yet the opening of the ampulla was obstructed. A resection of the head of the pancreas, duodenum, and antrum of the stomach was done.

In the specimen, the pancreatic duct ended in a duodenal papilla about 2 cm. proximal to the ampulla without an apparent opening.

Table 9. Pancreatic Juice in Operated Cases of Carcinoma of the Bile Ducts

Volume cc. Fractions 1	2	3	4	pH Fractions 1	2	3	4	Amylase Concentration Fractions 1	2	2	4	Protease Concentration Fractions 1	2	3	4	Lipase Concentration Fractions 1	2	3	4	Diagnosis and Remarks
24	10	11	28	7.5	7.5	7.5	7.5	+	+	+	+	+	+	+	+	+	+	+	+	Ca. lower ⅓ C.B.D. without involvement of ampulla
20	30	20	35	ac.	7.5	7.5	ac.	ac.	+	+	ac.	ac.	+	+		ac.	18	34	ac.	Ca. hepatic duct
16	11	13	8	7.5	7.5	7.5	7 5	+	+	+	+	+	+	+	+	3.4	10	15	15	Ca. C.B.D.
6	19	23	13	7.5	7.5	7.5	6.8	+	+	+	+	+	+	+	+	12	18	18	16	Ca. C.B.D.
25	17	6	15	7.5	7.5	7.5	7.5	+	+	+	+	+	+	+	+	15	17	16	14	Ca. C.B.D.
11	20	10	25	7.5	7.5	7.5	7.5	+	+	+	+	+	+	+	+	10	14	15	12	Ca. ampulla. P. duct entered 2 cm. above papilla and was patent. Blood in drainage
21	7	13	15	7.5	7.5	7 5	ac.	+	+	+	+	+	+	+	+	8.4	10.8	5.5	ac.	Ca. G.B. with nodes involving C.B.D.
29	69	39	49	ac.	7.5	7.5	ac.	ac.	+	+	ac.	+	+	+	+	ac.	21.7	8.4	ac.	Ca. common hepatic duct
7	13	2	16	8.1	8.1	8.1	7 9	+	+	+	+	+	+	l.	+	1	7	6	2	Ca. C.B.D.—P. duct not involved. Low lipase unexplained
14	15	9	5	7.3	7.6	7 6	7.6	+	+	+	+	+	+	+	+	12	12	12	12	Ca. common hepatic duct
	6.5	2	50	0	8.0	8.1	7.6	0	l.	l.	+	0	l.	l.	+	0	14.5	12.8	11	Ca. C.B.D.
20	9	8	4	7.2	8.1	8.1	8.3	+	+	+	+	+	l.	l.	l.	15	17	11	15	Ca. ampulla
25	13	5	30	7.5	7.9	8.3	6.9	+	+	+	+	+	+	+	+	13	14	13.7	13	Ca. C B.D. 2 cm. distal to cystic duct
44	12	8	35	7.0	7.0	7.5	7.0	.2	3	3	2	+	+	+	+	17	19	17	17	Ca. C B.D.
3	13	27	9	8.1	8.1	7.3	7.2	4.4	13.7	11.5	10.8	44.8	182	185	129	10	14	15	13	Ca. G.B. involving C B.D

56	22	44	34	7.0	7.1	7.0	7.0	2.9	4 9	5.6	4 6	35	51	66	75	8	10.7	9.9	8 5	Ca. ampulla with patent Santorini and Wirsung ducts
55	65	35	70	7.0	7 2	7.3	7 0	5.9	13 9	8.7	9 5	131	235	279	106	13.7	14.4	15	12.5	Ca. C.B.D.
0	19	6	45	0	6.7	7.3	7.5	0	2.6	3 8	6.4	0	39	20	101	0	8.6	6 6	13.1	Ca. ampulla No. pancreatic duct obstruction. Blood in pancreatic juice. Painless jaundice.
ac	39	22	ac.	—	7.3	7.5	—	—	7	3	—		139	91	—	—	14	10	—	Ca. C.B.D.
10.5	6.5	ac.	4 5	8.2	8 2	ac.	8.2	2 4	1	ac.	0.9	l.	l.	ac.	l.	.l	l.	ac.	l.	Ca. duod. at ampulla P. and C.B.D. dilated. Extreme fibrosis P. Stool—guiac+ 3 yr. later (Feb., 1948) well after mastectomy for ca. breast
20	23	45	20	7.5	8 1	7 4	7 2	5.9	5.7	4.1	7.0	+	+	+	+	14	15	14	15	Ca. duod. involving ampulla of Vater
								+	+	+	+	+	+	+	+	3	10	10	8	Ca. C.B.D.
86	24	2	0	7.0	7 0	7.0	0	0.2	0.3	0 1	—	18	12	11	—	1	1	1	1	Ca. of the papilla of Vater.
																				C.B. and P. ducts dilated. Microscopic—little fibrosis but marked dilatation of ducts Autopsy.
18	30	8	6	7.5	7 5	ac.	7.5	5	7	5	6	71	133	107	99	13	15	14	14	Ca. C.B.D.
15	16	19	20	7.1	6.7	7.0	6.5	3 4	8.5	6 3	7.1	106	207	165	193	14	16	15	16	Ca. C B.D. Autopsy

NOTE: All patients had obstructive jaundice.

Abbreviations: G.B =gallbladder
Ca.=cancer

l.=low
C.B.D.=common bile duct

P.=pancreas

Microscopically, however, a number of branching ducts penetrated the papilla, thus providing an outlet for the pancreatic juice into the duodenum (see Fig. 10).

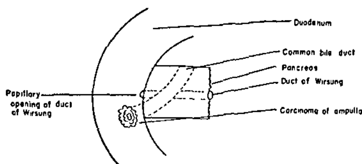


FIG. 10. Diagram of the specimen removed from patient 686471. The duct of Wirsung enters the duodenum through separate microscopic openings.

SPRUE

The malabsorption of foodstuffs, vitamins and minerals is responsible for the anemia, avitaminosis, low serum protein, low serum calcium, tetany, steatorrhea, diarrhea and emaciation so characteristic of this disease.

In most cases of adult sprue, the pancreas does not appear to be involved. To quote Comfort, Parker and Osterberg,[11] "the constant finding of pancreatic enzymes in normal amounts in cases of sprue is of considerable importance in the differential diagnosis" Childs and Dick[55] also found normal pancreatic juice in typical sprue. H. O. Lagerloef[6] cites two cases in which the pancreatic function test was of diagnostic value.

The investigation of A. C. Frazer and associates[56, 57] indicates that soluble soaps are absorbed by the portal blood vessels, and that finely divided fat enters the blood stream through the lymphatics. In sprue, the latter process, that is, the "particulate absorption" of fat, is interfered with. It is noteworthy that these authors found large numbers of bacteria in the upper part of the small intestinal tract only in cases of sprue.

In Table 10, fourteen cases of nontropical sprue are listed. All but one, about 93 per cent, had normal pancreatic ferment concentrations.

The first case was a man aged 33 who was admitted April 2, 1913, for intermittent diarrhea, which he had had all his life. He also had

Table 10. Pancreatic Juice in Nontropical Sprue*

Volume cc. Fractions				pH Fractions				Amylase Concentration Fractions				Protease Concentration Fractions				Lipase Concentration Fractions			
1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
19	22	40	25	7.5	7.5	7.5	6.9	1 0	+	+	+	+	1	+	+	–	1.0	0.8	9.
45	11	6	11	ac.	7 0	7.5	7.5	0	0	0	0	+	1	1	+	0	0	1.0	0 6
60	29	15	11 5	6.5	7.5	7.5	7.5	+	+	+	+	+	+	+	–	0 8	3.0	28.0	15.
8	21	32	55	8 0	7.6	7.5	6 1	+	+	+	+	+	+	1	1	1.0	12.0	11.0	0.7
60	63	23	75	7 5	7.5	7.5	7.5	0	1.	+	+	+	+	+	+	7.0	13.0	12.0	9.7
55	46	33	60	6 3	6.8	ac.	ac.	+	+	+	0	+	+	+	+	13	18.0	17	4 0
5	21	16	7	7 9	7.9	7.7	7.9	1.0	+	+	+	+	+	+	+	5	14	14	15 0
25	15	31	12	7 7	7 9	7.8	7.8	+	+	+	+	+	+	+	+	11	14	13	12
49	85	27	23	6 9	7 2	7 2	6 4	+	+	+	+	+	+	+	+	14	18	19	12
10	20	23	22	7 9	8 0	7.0	7 3	5	10	10	11	+	+	+	+	18	22	22	22
7.	9.5	12	5	6 2	7 6	7.8	8.0	–	15	15	18	–	255	302	400	1	15	17	17
6	23	33	8 9	7 5	7.5	7.5	7.5	5 5	9	10.8	7.8	61	237	273	25	12	14.5	17	7.6
25	15	31	12	7.7	7 9	7 8	7.8	+	+	+	+	+	+	+	+	11.2	13.7	13	11.8
20	16	6 5	3	7.7	7.7	7.8	7.7	9	9 6	13.5	15.2	160	188	321	276	9.4	9.1	11.3	10.4
30	4.0	1.5	20	7 4	7.4	7.4	7.4	1 6	3.2	1 4	21.0	93	203	68	93	7	13	5	5

Minimum normal values: Amylase 4
Protease 50
Lipase 8

had clubbing of the fingers and toes as long as he could remember. Additional symptoms were weakness, stiffness in the arms and legs and polyuria. Roentgen examination showed a marked deficiency pattern of the small intestine. Colon roentgenogram was negative. Stool was negative for ova and parasites. Serum calcium was 4 mg. per cent, serum albumin 5.4, and globulin 2.6. The glucose tolerance curve was flat, fasting blood sugar 91, ½ hour 91, 1 hour 103, 2 hours 75, and 3 hours 82. Anacidity after histamine injection. The red blood count was 3,520,000, the hemoglobin 12 grams per cent, and the white count was 8,700. The pancreatic juice was essentially normal. The fat absorption was 87 per cent. Urine was negative.

While in the hospital under treatment, his food consumption reached 5,000 calories, his weight increased by 15 pounds, and the serum calcium rose to 8.7 mg. per cent. By March, 1945, his initial weight of 110 had risen to 154 pounds and his serum calcium to 9.1. Relapses occurred when he went off his diet. In June, 1946, he entered the hospital in a depleted state and died of a terminal pneumonia. Autopsy showed a normal pancreas and marked atrophy of the alimentary canal.

Pernicious Anemia

In pernicious anemia, the absence of hydrochloric acid prevents gastric digestion and deprives the patient of the secretin activator. It therefore seemed desirable to ascertain the pancreatic response to the vagus stimulant, mecholyl, in this condition. According to Table 11, the pancreatic juice was normal in seven of eight pernicious anemia patients.

Table 11. Pancreatic Juice in Pernicious Anemia

Volume cc. Fractions				pH Fractions				Amylase Concentration Fractions				Protease Concentration Fractions				Lipase Concentration Fractions			
1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
9	12	7	9	7.9	8 0	7.5	–	+	+	+	+	+	+	+	1.	13	17	23	23
2	15	8	58	7.0	7.5	7.5	7.5	+	+	+	+	+	+	+	1.	2	16	17	16
21	12	10	3	7.8	7.8	7.9	7.9	+	+	+	+	+	+	+	+	11	17	14	12
10	21	78	35	7.9	7.6	7.7	7.8	+	+	+	+	1.	1.	+	+	0.5	0.5	0.8	13
15	17	6	–	7.2	7.5	7.6	–	+	+	+	–	+	+	+	–	14	23	21	–
5	14	45	7	7.9	7.8	7.6	8 0	+	+	+	+	–	1.	+	+	0.47	2	3	3
29	15	49	12	7.6	7.7	7.7	8.0	+	+	+	+	+	+	+	+	6	6	14	12
8	18	6 4	17 5	7.7	7.9	7.5	7.8	11	22	17	20	81	98	96	82	5	17	11	8.7

Minimum normal values: Amylase 4
Protease 50
Lipase 8

PART II

Fat Absorption Studies in Pancreatic Deficiency

In the absence of jaundice, the determination of fat absorption is of diagnostic value in pancreatic disease.

The results of fat balance studies in man after removal of the head of the pancreas or the entire organ have been surprisingly variable.[59, 60] They are comparable to the experience in dogs deprived of their pancreatic juice.[58] Brunschwig[61] resected the head of the pancreas and tied off the ducts in two macacus rhesus monkeys. The one lived normally for 1 year and was then sacrificed. The liver was normal; the body and tail of the pancreas formed a cyst but many of the islands of Langerhans were well preserved The other animal lived in excellent condition for 14 months on the usual diet.

TABLE 12. THE FAT ABSORPTION IN 7 PATIENTS IN WHOM THE HEAD OF THE PANCREAS AND DUODENUM OR THE ENTIRE GLAND HAD BEEN REMOVED

PATIENT No	PANCREATECTOMY	FAT INTAKE GRAMS	ABSORPTION FAT %
1	Partial	100	96 8
2	Partial	130	89.0
3	Partial	75	87.0
4	Partial	75	25 0
4	Partial	75	92 0—Taking 9 capsules pancreatin o d.
5	Complete	75	75 0
5	Complete	75	81 0—Taking 15 capsules pancreatin o d.
6	Complete	70	48 6
7	Complete	100	51 0

Of the seven patients without pancreatic juice, three had normal fat absorption. In two others, the absorption became satisfactory when

dried pancreas was added to the diet. Cases 6 and 7 were reported from the Mayo Clinic.[22] This individual variation is inexplicable at the present time. *According to Free and Myers,[28] human intestinal juice* obtained from an isolated segment of intestine with a Miller-Abbott tube possessed no ferment activity.

Even in completely depancreatized dogs, Vermeulen et al.[85] found that the absorption of triolein varied considerably.

A number of observers[22, 32, 58] have noted a gratifying increase in fat absorption following the use of dried pancreas in cases of pancreatic juice deficiency. *Most recently, additional fat and protein ab*sorption studies were done on ten patients after resection of the head of the pancreas. Absorption was better when the pancreatic duct was reunited with the small intestine than when it was ligated. The beneficial effect of giving dried pancreas with meals was confirmed.[62]

DETERMINATION OF FAT IN THE STOOL

The patient is given a diet of 200 carbohydrate, 70 protein and 75 grams of fat.

After several days, a purgative, for example, 0.6 of cascara or 20 Gm. epsom salts, is administered, and the resulting stool is discarded. During the following three days, the stool is collected, united, emulsified with water by means of an electric stirrer and then diluted to a convenient volume. An aliquot of from 10 to 20 cc. is used for the fat determination. It is introduced into a 100-cc. separating funnel, and 1 cc. of concentrated hydrochloric acid and 20 cc. of water are added. The fat is extracted with successive 20-cc. portions of ether until evaporation of a small amount of ether extract leaves no residue. A little alcohol may be added to facilitate the separation of the ethereal from the aqueous layer. The ether extracts are evaporated. The residue is dried in a vacuum desiccator, and then extracted three times with petroleum ether. The combined extracts are united and filtered into a weighed beaker of from 100 to 150 cc. capacity. The filter paper is washed with petroleum ether. The extract is evaporated and dried in a vacuum desiccator and weighed.

$$\frac{\text{Total Volume of Fecal Emulsion} \times \text{Weight of Fat in Aliquot}}{\text{Volume of Aliquot}} = \text{Fat in 3 days' stool}$$

PART III

Serum Amylase

The starch-splitting activity of the serum is due to amylases chiefly elaborated by the pancreas and salivary glands. Total extirpation of the pancreas causes an immediate 50 per cent decrease in serum amylase activity.[63]

The amount (or percentage) of reducing sugar liberated by a known quantity of serum from a known amount of starch is the index of amylolytic activity. In the hospital laboratory, we have used the method of Myers and Killian.[64] The results are expressed as the percentage of 10 mg. or more of starch converted into sugar by 2 cc. of serum.

SERUM AMYLASE DETERMINATION

It is important to guard against the entrance of saliva into the measuring pipettes by aspirating through a connecting rubber tube containing cotton wool.

Solutions Required:

1. A standard solution of 0.02 per cent glucose in saturated picric acid is stored in the refrigerator in a brown glass bottle.

2. Saturated picric acid solution is prepared by dissolving approximately 1.5 Gm. picric acid in 100 cc. of water Mix, allow to dissolve overnight, filter, and preserve in a brown bottle.

3. A 1 per cent starch solution is prepared by making a paste of 1 Gm. of soluble starch with a few drops of cold water and adding about 95 cc. of boiling distilled water. Cool and bring to volume. The solution keeps for about two weeks in the refrigerator.

Method: Prepare four tubes as follows:

Tube A 0 5	*Tube B*
0 5 cc serum	2 cc serum
8 5 cc. distilled water	7 cc distilled water

dried pancreas was added to the diet. Cases 6 and 7 were reported from the Mayo Clinic.[22] This individual variation is inexplicable at the present time. According to Free and Myers,[28] human intestinal juice obtained from an isolated segment of intestine with a Miller-Abbott tube possessed no ferment activity.

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$$\frac{\text{Total Volume of Fecal Emulsion} \times \text{Weight of Fat in Aliquot}}{\text{Volume of Aliquot}} = \text{Fat in 3 days' stool}$$

Two cc. of normal serum contains from 10 to 30 Myers and Killian units, comparable to from 16 to 36 Somogyi units.

The test is rather simple, and the results can be obtained in from one-half to one hour, depending on the experience of the technician. Recently, Myers, Free and Rosinski[65] have modified the original method.

In acute inflammation of the pancreas or salivary glands, the swollen tissue obstructs the duct system sufficiently to increase the rate of ferment reabsorption and thus raise the level of amylase in the serum. Rarely is the destruction of parenchyma so extensive that ferment production is reduced sufficiently to lower the serum amylase level.

In 1908, Schlesinger[66] observed a rise in the blood amylase in rabbits after tying off the pancreatic duct. About the same time, Wohlgemuth[67] discovered an increase of amylase in the urine in acute pancreatitis. In advanced renal disease, retention may cause an elevation of amylase in the blood.

The diagnostic value of the determination of amylase in the serum in acute pancreatitis was pointed out by Elman and associates[68] 20 years ago and has been amply confirmed by subsequent workers.

Since good surgical judgment is opposed to immediate intervention in most cases of acute pancreatitis, the estimation of serum amylase has become a decisive and important diagnostic procedure. It is also valuable in determining involvement of the pancreas in upper abdominal injuries.

Difficulty in the differential diagnosis of acute upper abdominal conditions is a common experience in the surgical emergency service of a large hospital. Before the introduction of the serum amylase test, French observers[48] report that in 468 cases of acute pancreatitis, a preoperative diagnosis was stated in 192, and of these only 39 were correct. Though not nearly as common as appendicitis, gallbladder disease, perforated duodenal ulcer, or intestinal obstruction, acute pancreatitis is a possibility that merits consideration. With rare exception, an elevated serum amylase is conclusive evidence of pancreatic edema or inflammation.

In the tables that follow, the serum amylase values in about 400 patients have been correlated with other laboratory and clinical data and tabulated according to the underlying disease.

Some patients were followed for over ten years in the outpatient

Tube A 1
1 cc. serum
8 cc. distilled water

Tube A 2
2 cc. serum
7 cc. distilled water

Place these and a tube containing approximately 5 cc. of starch solution in a bath at 40° for ten minutes. Clear the starch solution by heating before using and place a stirring rod in each tube. Add 1 cc. of starch to tubes A 0.5, A 1, and A 2. Incubate in constant temperature water bath for exactly fifteen minutes, mixing well, then immerse the tubes in an ice bath and add from ½ to 1 Gm. of solid picric acid. Stir well, and keep in the ice bath until each tube has a uniform yellow color; then add 1 cc. of starch to the blank tube B. Filter all four tubes through regular Whatman filter paper. Place 3 cc. of each filtrate in a Folin-Wu sugar tube and 3 cc. of the standard in a fifth tube. Add 1 cc. of 20 per cent sodium carbonate to each tube; shake vigorously and heat in a boiling water bath for fifteen minutes. Cool. Dilute the tubes to the 25 cc. mark with distilled water and read in the colorimeter. The color is stable.

Calculations. Set the standard at 20.

Tube A 0 5

$$\frac{20}{R} \times 0\ 6^{a} \times \frac{1}{0.15_{b}} = \text{Total mg glucose per cc of serum or blood}$$

Tube A 1

$$\frac{20}{R} \times 0.6^{a} \times \frac{1}{0.3_{b}} = \text{Total mg. glucose per cc of serum or blood}$$

Tube A 2

$$\frac{20}{R} \times 0.6^{a} \times \frac{1}{0\ 6_{b}} = \text{Total mg. glucose per cc. of serum or blood}$$

Tube B
Same as Tube A 2

R = Reading of unknown
a = Amount of glucose in standard glucose solution
b = Amount of serum used

The amylase value in units is obtained by subtracting the results of B tube from the average of the three A tubes and multiplying by 20.

Patient No. 6 of the unoperated group was of special interest. He had received a single massive dose of arsphenamine for syphilis which resulted in inflammation of the brain, liver and pancreas. Branch[71] described a similar case of pancreatic necrosis following the application of arsenious acid paste to a patient with carcinoma of the breast. The diagnosis was verified at necropsy.

The advantage of delaying operation in acute pancreatitis is illustrated by the behavier of two men, history No. 713114 and No. 748633, who were admitted to the surgical ward at the same time with the classical, clinical and laboratory features of acute pancreatitis. E. R., aged 54, had severe epigastric pain, tenderness, fever, vomiting and a white blood count of 28,000.

Serum Amylase

6/11	120	6/15	33
6/12	142	6/19	34
6/12	216	6/27	36
6/13	173	7/2	83
6/14	94		

On July 3rd, about three weeks after admission, a mass in the left epigastrium became palpable. One thousand cc. of purulent fluid were removed from the lesser sac, and this was followed by recovery.

The second patient, T. H., aged 40, had epigastric pain associated with nausea and vomiting, spasm in the right upper quadrant, tenderness in the epigastrium, fever and a white blood count of 17,000.

Serum Amylase		*Serum Bilirubin*	*Serum Lipase*
6/11	130	trace	normal (1.2 cc.)
6/12	110		
6/14	46		
6/19	92		
6/26	46		

On June 26th he was asymptomatic. Cholecystogram was normal. He was discharged. He was in good health six months later.

More rarely, the condition is very serious, with widespread hemorrhage and necrosis accompanied by shock, spreading peritonitis and exitus.

department; in others, additional information was obtained at a later operation or at autopsy.

SERUM AMYLASE IN ACUTE PANCREATITIS

The values in 47 operated cases (see Table 13) confirm the well known elevation of serum amylase in acute edema and inflammation of the pancreas. Lagerloef[6] found the amylase elevated in 21 patients with acute and chronic relapsing pancreatitis. A decline to normal levels is apt to occur in 48 hours. This may be the result of rapid excretion by the kidney, subsidence of the edema or inflammation, or relief of blockage of the ampulla of Vater by a movable stone, or relaxation of spasm of the sphincter of Oddi. The decline in serum amylase may not coincide with clinical subsidence of the inflammatory features. Acute edema may disappear so rapidly that at operation a few days after onset, no abnormality of the pancreas is found.

Occasionally, the elevation persists without other clinical or laboratory evidence of continued inflammation.

Bilirubinemia is frequent, though not invariable. It results from pressure on the common bile duct or concomitant blockage by stone.

The association of pancreatitis with stones in the gallbladder is frequent. Brocq[48] found stones in the common bile duct in 146 of 228 explored cases of pancreatitis (64 per cent). Of these only 11 had a stone wedged in the ampulla. Griesmann[69] found that 94 per cent of acute pancreatitis cases had gallbladder or biliary duct disease and 79 per cent had stones in the gallbladder.

If possible, a cholecystogram should be done in every case before discharge. If stones in the gallbladder are present, cholecystectomy usually prevents future attacks. Recurrences after removal of the gallbladder are probably due to lighting up to residual foci of infection within the pancreas or neighboring lymphatics.

Evidence is accumulating that alcohol indulgence is a causal factor in both acute and chronic pancreatitis.[70,71] Carter[72] found edema of the pancreas in alcoholics with abdominal symptoms and an elevated serum amylase. Clark[70] cites 36 cases of pancreatitis in alcoholics with cirrhosis or fatty liver. (See also Weiner and Tennant.[73])

The restoration of pancreatic function after an acute attack is usually complete, unless the process has been too severe and extensive or preceding bouts have caused widespread replacement of parenchyma by fibrous tissue.[38]

TABLE 13 (*Continued*). SERUM AMYLASE VALUES IN OPERATED CASES OF ACUTE PANCREATITIS

No	Serum Amylase	Days Later	Serum P'tase	Serum Bili.	Condition Found at Operation
27	146		13.	4.8	P. firm
28	39		14.	7.4	Nodules head of P., stones in gallbladder
29	138				2 days after removal body and tail of P.
30	129				Blocked drainage, marsupialized cyst
31	88				Ac. pctis. with fat necrosis
32	82		3.	1.	Ac. pctis. with fat necrosis, gallbladder normal
33	37		17.	3 8	P. large and hard, biopsy = fibrosis, stones in gallbladder
34	143			3.9	P. enlarged, edematous
35	208		4.	2.1	Head P. enlarged, nodular, stones in gallbladder
36	122		39.	1.9	Ac. pctis, pancreatic cyst, stones in gallbladder
37	191				P. firm, stones in gallbladder
38	160		17.4	6 4	P. enlarged, stones in gallbladder
39	42				[illegible]
40	41			2.	[illegible]
41	116				[illegible]
42	133	(Ser. Lipase = 17.4)	10.7	5.1	P. felt normal
43	380				P. enlarged, stones in gallbladder
43	8	3			
44	99				1 day post partial p'ectomy for ca. of papilla Vater, autopsy = Fat necrosis around cut end of P.
45	90				Much edema about gallbladder, stones in gallbladder, P. unexplored
46	50				Stones in gallbladder, P. felt normal, F. U. 9 yrs. = patient well
47	61			2 6	Stones and ca. gallbladder, P felt normal F. U. 11 yrs = patient well
47	36	2			
47	26	8			

TABLE 13. SERUM AMYLASE VALUES IN OPERATED CASES OF ACUTE PANCREATITIS

No.	Serum Amylase	Days Later	Serum P'tase	Serum Bili.	Condition Found at Operation
1	186		4.6	3.7	Ac. pctis. fat necrosis, ac. gangrenous cholecystitis
1	112	1			
1	16	2			
2	52			14.	Head P. enlarged, fat necrosis, stones in gallbladder
3	74			11.9	Hemorrhagic pctis., fat necrosis, stones in gallbladder
4	137				Acute pctis., fat necrosis, stones in gallbladder
4	114	1			
5	88				Edema and abscess head of P., gallstones
6	66			Trace	Abscess P.
7	76		3.8		P. enlarged, cyst formation
8	229		13	3.	Indurated head P., stones in gallbladder
8	28	3			
9	82		3.	1.	Abdominal exudate, fat necrosis
9	27	2			
10	64				P. abscess
11	94				Ac. pctis., fat necrosis
12	91			3.6	Ac. pctis., stones in gallbladder
13	165		8.1	7.	Nodular enlarged P.
13	100				Bullet wound P. and stomach
14	244		4.		P. head hard, stones in gallbladder
14	288				2nd attack 8 mos after cholecystectomy
15	100				Bullet wound P. and stomach
16	199			1.7	Ac. necrotic pctis (autopsy)
17	172		8.	1.5	P. enlarged, stones in gallbladder
17	27	2			
18	87		7.	11.	Nodular masses in P., stones in gallbladder
19	216				Ac. pctis., abscess in lesser sac
19	33	3			
20	96				First day after partial resection P. for adenoma
20	43	2			
21	134				Head P. enlarged, fat necrosis
21	45	2			
22	80				Head P. enlarged, fat necrosis
23	70				Head P. very large, stones in gallbladder
23	19	2			
24	174				P. firm, several nodules in head, stones in gallbladder
24	32	2			
25	130				Fat necrosis, stones in gallbladder
26	102			3.	Nodules body and head of P.

TABLE 14 (*Continued*). SERUM AMYLASE IN UNOPERATED CASES OF ACUTE PANCREATITIS

No.	S.A.	Days Later	Serum P'tase	Serum Bili.	Gall-bladder X-ray	Wbc.	Clinical Features and Remarks
14	204			1.1			Gallbladder out 3 wks ago, now epig pain, vomiting, jaundice, P. function test normal
14	54	3					
15	87		7.0	11.0	Abnormal		R.U Q. pain, jaundice, P. function test normal
16	59				Normal	5,250	Epig. pain, gallbladder out 2 mos ago
17	49		48.	3.5			R U.Q. pain after cholecystectomy
18	50					20,000	L U.Q. pain
19	71				Appearance of intest. obstruction	19,250	Mid abd. pain, fever, epig. tender, gallbladder out 5 yr. ago, P. = normal, F U 2 yr. bouts of abd. pain. In Mar , 1948, developed ac necrotic pancreatitis with fat necrosis
19	34	4					
20	77		6 3	Trace	Abnormal	23,800	R U Q pain, vomiting
21	57						Epig. pain, vomiting, gallbladder out 3 mos ago, P function test—normal
22	59		11 2	5 7		20,300	R U.Q pain, vomiting, jaundice, stones in common bile duct and G B.—Op 6 mos ago
22	41						
23	66		12 3	2 1	Pressure on duodenum		P. function test—abnormal
	8	4					
24	156			Trace	Normal		Epig. pain, alcoholic, P. function test abnormal, F U. 6 mos patient well
24	70	1					
25	13						Cholecystectomy g s R U Q. pain 3 days after op. F U 1 mo. satisfactory
	112						
	32	7					
26	86						Epig. pain, vomiting, mass in epig tender, ac pctis, absorption of contents false cyst
	12	4					

TABLE 14. SERUM AMYLASE VALUES IN UNOPERATED CASES OF ACUTE PANCREATITIS

No.	S.A.	Days Later	Serum P'tase	Serum Bili.	Gall-bladder X-ray	Wbc.	Clinical Features and Remarks
1	76			Trace	Normal	14,600	Epig pain, fever, tender abdomen
1	7	4					
1	199						Recurrence 7 yrs. later
2	47			4.7	Abnormal	5,200	Epig. pain, fever
3	79						L.U Q. *pain, fever, stones*
3	45	2					L.U Q. tender
4	75		10.4	Trace	Normal	16,500	Epig pain, F.U =minor pains for several years, indeterminate
	71	6					
5	66					13,500	Attacks epig. pain for 16 yrs., pancreatic function test abnormal—recurring pctis.
5	45	7	11.4	Trace			
6	250						Abd. pain after intensive arsphenamine treatment, pctis, hepatitis, encephalitis, normal pancreatic function test
6	192	2					
7	200					19,650	R.U Q pain, 1 mo. after cholecystectomy F.U.= no symptoms
7	37						
7	34						
8	75					12,000	Epig. pain
	45	2					
9	66				Normal		Epig R.U Q pain, pancreatic function test normal
	54	3					
10	200			2.1			Epig. pain, gallbladder out for stones 1 mo. ago, F.U. 18 yrs, no recurrence
	39	3					
11	127					20,200	Abd. pain, vomiting
12	117		3.7	0 5			Gallbladder out for stones, 1 mo. later pain, vomiting, common bile duct in satisfactory condition
12			9 0				
13	64			2 4		20,300	R U Q. and L U.Q. pain, vomiting, jaundice, had cholecystectomy in past

TABLE 15. SERUM AMYLASE IN CHRONIC PANCREATITIS

No.	Serum Amylase	Serum P'tase	Serum Bili.	Pancreatic Function Test	Findings at Operation—Pancreas
1	31			Abnormal	Hard, nodular P.
2	32			Abnormal	Fibrosis, calcification
3	31		Trace		Hard, nodular
4	51		Trace	Abnormal	Unoperated
5	28			Abnormal	Fibrosis, calculi
6	42			Abnormal	Fibrosis, calculi
7*	16		1.7		Fibrosis, fat necrosis
8	22			Abnormal	Unoperated
9	63		Trace		Fibrosis (biopsy)
10	31			Abnormal	Fibrosis, calcification
11	39	14.	7.4	Abnormal	Fibrosis, gallstones
12	49				Fibrosis, gallstones
13	8	6	3 0		Fibrosis, necrosis gallstones
14	21			Abnormal	Fibrosis, calcification
15	32				Fibrosis, gallstones
16	26			Abnormal	Unoperated
17	39			Abnormal	Fibrosis, calcification
18	10			Abnormal	Unoperated
19	20		4.7		Fibrosis (biopsy)

*The serum amylase determined between attacks

found in the same conditions and during the same period of time as an elevated amylase. He prefers the latter, as it is less time-consuming and more accurate. McCall and Reinhold[76] also found that in cancer of the pancreas the serum lipase was more frequently elevated than the amylase and suggest that a normal amylase, associated with an elevated lipase, points to cancer.

An obvious element in the controversy is the lack of agreement amongst authors about the upper normal limit of serum amylase concentration. For example, Comfort and Osterberg[74] accept 320 Somogyi units, which is about twice as high as the commonly observed value in nonpancreatic disease. Final judgment will be possible when more figures are available. It is conceivable that amylase is more rapidly eliminated by the kidneys than lipase.

A probable case of cancerous proliferation of functioning acinar tissue is described by M. W. Comfort and associates.[77] It was characterized by extremely high concentrations of serum amylase and lipase.

TABLE 14 (*Continued*). SERUM AMYLASE IN UNOPERATED CASES OF ACUTE PANCREATITIS

No.	S.A.	Days Later	Serum P'tase	Serum Bili.	Gall-bladder X-ray	Wbc.	Clinical Features and Remarks
27	90		15.5	3.2			R.U.Q. epig. pain tender, autopsy 8 yrs. later P. normal, stone gallbladder
28	100						1 mo. after cholecystectomy *for gallstones epig pain,* vomiting
29	123						Epig. R.U Q. pain, stones gallbladder, P. normal
30	43			2.0			Epig. pain, stones gallbladder, P. *not explored*
31	39				Abnormal		R.U.Q. pain, vomiting, stones, gallbladder perforated
32	107			5.2			R.U.Q. pain, 1 mo. later gallbladder *out. Stones*
33	72				Normal		Mid. abd. pain, fever, F.U. = no symptoms
34	191				Stones in gallbladder		Epig. L.U.Q. pain, stones in gallbladder 5 wks. later P. firm
35	129			2 2			Blocked drainage, P. cyst posttraumatic
35	25	9					

THE SERUM AMYLASE IN CHRONIC PANCREATITIS

The serum amylase in chronic pancreatitis is usually below or slightly above the upper limit of normal (30). In this condition, the pancreatic function test is of greater diagnostic value. If sufficient uninvolved acinar tissue remains, the serum amylase rises during acute relapses or during subacute smoldering activity.

SERUM AMYLASE IN CANCER OF THE PANCREAS

The serum amylase was above normal in about one half of the cases (Table 16). *Seventeen of the 22 cases were jaundiced.* The serum amylase and pancreatic ferment values are influenced by the site and size of the tumor. *Comfort and Osterberg*[74] *found that the serum* lipase was more frequently elevated in carcinoma than the serum amylase, whereas Lagerloef[75] states that an elevated serum lipase is

TABLE 17. SERUM AMYLASE IN OPERATED GALLBLADDER DISEASE

No.	Serum *Amylase*	Serum *Bilirubin*	Findings at Operation
1	29		Stones in gallbladder
2	27		Stones in gallbladder
3	29		Chr. cholecystitis, head of P. normal
4	25		Stones in gallbladder, head of P. normal
5	27		Stones in gallbladder
6	16	16.5	Ca. gallbladder and liver
7	27		Acute cholecystitis
8	23		Stones in gallbladder
9	16		[illegible]
10	20		[illegible]
11	21	1.8	[illegible]
12	23		[illegible]
13	16		[illegible]
14	15		[illegible]
15	13		[illegible]
16	29		Stones in gallbladder, P. normal
17	15		Stones in gallbladder
18	29		Stones in gallbladder
19	17		Acute cholecystitis
20	25	2 6	Stones in gallbladder, P. [illegible]
21	12		[illegible]
22	23		[illegible]
23	23	4.2	[illegible]
24	16		Stones in gall bladder
25	13		Stones in gallbladder
26	16		Stones in gallbladder, P. normal
27	14		Stones in gallbladder
28	20		Stones in gallbladder, Ca gallbladder
29	39		Stones in gallbladder, P normal
30	35		Stones in gallbladder
31	34	Trace	Stones in gallbladder
32	33		Stones in gallbladder
33	39	13 6	Stones in gallbladder, Ca. common bile duct
34*	53		Stones in gallbladder
35†	120		Stones in gallbladder, P. normal
36	39		Stones in gallbladder
37	31	32	Stones in gallbladder, Common bile duct thick—F U. 8 yrs. O K.
38	33		Stones in gallbladder, P. normal
39	35		Stones in gallbladder
40	31		Stones in gallbladder
41	33		Stones in gallbladder
42‡	48		Stones in gallbladder

*The elevated amylase occurred 8 days after cholecystectomy for stones and was accompanied by epigastric pain, vomiting and jaundice

†*Cholecystectomy* 18 days after amylase determination.

‡Epigastric pain and serum amylase 44 three years before

TABLE 16. SERUM AMYLASE IN CANCER OF THE PANCREAS

No.	Serum			Pancreatic Function Test	Findings at Operation
	Amylase	*P'tase*	*Bili.*		
1	47		2.8	Normal	Ca. of the duodenum and head of P.
2	36		2.7	Abnormal	Ca. entire P.
3	55			Normal	Movable mass head P.
4	87	18	11.5	Abnormal	Ca. head of P.
5	108	9	9.2	Abnormal	Ca. duodenum blocked P. duct, secondary fibrosis P.
6	52			Normal	Ca. stomach involving P.
7	37	19	10.	Abnormal	Ca. P., metastases to peritoneum
8	67	36	6 9		Ca. head P.
9	52	18	18.5		Ca. head and body P.
10	81				Ca. entire P.
11	18	17	6.9	Abnormal	Ca. head of P.
12	12	22	12.		Ca. head of P.
13	15				Ca. P., metastases liver, peritoneum (autopsy)
14	25	19	11.	Abnormal	Ca. head and tail P. (autopsy)
15	10	9.4	6.8		Ca. head of P.
16	24	24	11.3	Abnormal	Ca. ampulla vater
17	27				Retroperitoneal mass, metastases liver, possibly ca. body P.
18	21	14.5	8 2		Ca. head P.
19	25	22	12.6	Abnormal	Ca. head P.
20	30	19.6	13.	Normal	Ca. head P.
21	16	32	9.6	Abnormal	Ca. ampulla, partial occlusion P. duct. Biopsy = fibrosis.
22	29	34	24.		Ca head P.

SERUM AMYLASE IN OPERATED CASES OF GALLBLADDER DISEASE

In 42 operated cases of gallbladder disease (Table 17), the serum amylase was under or slightly over 30. In several jaundiced patients, exploration of the common bile duct was negative; in 12, palpation of the pancreas was also negative. Transitory edema of the head of the pancreas probably accounts for the occasional rise of amylase in this condition.

While stones in the gallbladder are common in pancreatitis, pancreatitis is uncommon in the ordinary case of gallstones. It is more likely to occur in the long-standing cases with pericholecystitis and lymphatic spread.

TABLE 17. SERUM AMYLASE IN OPERATED GALLBLADDER DISEASE

No.	Serum Amylase	Serum Bilirubin	Findings at Operation
1	29		Stones in gallbladder
2	27		[illegible]
3	29		
4	25		"
5	27		"
6	16	16.5	
7	27		Acute cholecystitis
8	23		Stones in gallbladder
9	16		Stones in gallbladder
10	20		Cholesterosis of gallbladder
11	21	1.8	Stones in gallbladder
12	23		Stones in gallbladder, P. normal
13	16		Stones in gallbladder, P. normal
14	15		Stones in gallbladder
15	13		Stones in cystic duct, residual
16	29		Stones in gallbladder, P. normal
17	15		Stones in gallbladder
18	29		Stones in gallbladder
19	17		Acute cholecystitis
20	25	2 6	[illegible]
21	12		
22	23		
23	23	4.2	Stones in gallbladder, P. normal, common bile duct dilated
24	16		Stones in gall bladder
25	13		Stones in gallbladder
26	16		Stones in gallbladder, P normal
27	14		Stones in gallbladder
28	20		Stones in gallbladder, Ca gallbladder
29	39		Stones in gallbladder, P. normal
30	35		Stones in gallbladder
31	34	Trace	Stones in gallbladder
32	33		Stones in gallbladder
33	39	13 6	Stones in gallbladder, Ca. common bile duct
34*	53		Stones in gallbladder
35†	120		Stones in gallbladder, P. normal
36	39		Stones in gallbladder
37	31	32	Stones in gallbladder, Common bile duct thick—F U. 8 yrs. O K.
38	33		Stones in gallbladder, P. normal
39	35		Stones in gallbladder
40	31		Stones in gallbladder
41	33		Stones in gallbladder
42‡	48		Stones in gallbladder

*The elevated amylase occurred 8 days after cholecystectomy for stones and was accompanied by epigastric pain vomiting and jaundice

†Cholecystectomy 18 days after amylase determination

‡Epigastric pain and serum amylase 44 three years before

TABLE 16. SERUM AMYLASE IN CANCER OF THE PANCREAS

No.	Serum Amylase	Serum P'tase	Serum Bili.	Pancreatic Function Test	Findings at Operation
1	47		2.8	Normal	Ca. of the duodenum and head of P.
2	36		2.7	Abnormal	Ca. entire P.
3	55			Normal	Movable mass head P.
4	87	18	11.5	Abnormal	Ca. head of P.
5	108	9	9.2	Abnormal	Ca. duodenum blocked P. duct, secondary fibrosis P.
6	52			Normal	Ca. stomach involving P.
7	37	19	10.	Abnormal	Ca. P., metastases to peritoneum
8	67	36	6.9		Ca. head P.
9	52	18	18.5		Ca. head and body P.
10	81				Ca. entire P.
11	18	17	6.9	Abnormal	Ca. head of P.
12	12	22	12.		Ca. head of P.
13	15				Ca P., metastases liver, peritoneum (autopsy)
14	25	19	11.	Abnormal	Ca. head and tail P. (autopsy)
15	10	9.4	6.8		Ca. head of P.
16	24	24	11.3	Abnormal	Ca. ampulla vater
17	27				Retroperitoneal mass, metastases liver, possibly ca. body P.
18	21	14 5	8 2		Ca. head P.
19	25	22	12.6	Abnormal	Ca. head P.
20	30	19.6	13.	Normal	Ca. head P.
21	16	32	9 6	Abnormal	Ca ampulla, partial occlusion P. duct. Biopsy = fibrosis.
22	29	34	24.		Ca. head P.

SERUM AMYLASE IN OPERATED CASES OF GALLBLADDER DISEASE

In 42 operated cases of gallbladder disease (Table 17), the serum amylase was under or slightly over 30. In several jaundiced patients, exploration of the common bile duct was negative; in 12, palpation of the pancreas was also negative. Transitory edema of the head of the pancreas probably accounts for the occasional rise of amylase in this condition.

While stones in the gallbladder are common in pancreatitis, pancreatitis is uncommon in the ordinary case of gallstones. It is more likely to occur in the long-standing cases with pericholecystitis and lymphatic spread.

SERUM AMYLASE IN PATIENTS WITH STONE IN THE COMMON BILE DUCT

The amylase was above normal in 28 of 40 patients (70 per cent) with stone in the common duct. The surgeon examined the pancreas in 19 of these 28 patients. He found induration, enlargement or fat necrosis in 15 (79 per cent). As in acute pancreatitis without common duct stone, the decline of serum amylase was usually rapid.

In 26 patients (65 per cent), measurable amounts of bilirubin were found in the serum.

Pancreatic function tests were carried out in 12 patients: 8 were normal (66 per cent). The association of pancreatitis with common duct stone is frequent. The generally accepted cause of this complication is the entrance of bile into the pancreatic duct, the so-called common channel theory. In support of this time-honored conception is the fact that in human cholangiograms the contrast medium injected into the common bile duct occasionally enters the pancreatic duct. Leven[37] saw the pancreatic duct in 23 per cent of 91 cholangiograms. In a few instances, actual blockage of the opening of the pancreatic duct by a stone in the ampulla may account for an elevated amylase. The follow-up experience indicates that removal of the stone results in permanent cure in the larger number of patients.

TABLE 19. NORMAL SERUM AMYLASE IN PROVED CASES OF COMMON DUCT STONE

No.	Serum			Pancreatic Function Test	Condition of Head of Pancreas at Operation	Remarks
	Amylase	*P'tase*	*Bili.*			
1	13	21.0	1.6		Normal	
2	16	7.9	9.4	Abnormal	Normal	
3	30	7.3			Abnormal	
4	28			Normal		
5	22				Abnormal	
6	17				Normal	
7	12	4.0	3.2		Normal	
8	16		5.1		Abnormal	
9	12	6.0	12.5		Normal	
10	15		5.4			F.U. 6 yrs. uneventful
11	23	8.4	6.3			Serum lipase 1.2 (normal)
12	12		8.1			F.U. 5 yrs uneventful

Table 18. Elevated Serum Amylase in Operated Cases of Common Bile Duct Stone

No.	S.A.	Days Later	Serum *Phosphatase*	Serum *Bilirubin*	Pancreatic Function Test	Condition of the Head of Pancreas	Remarks
1	38			39.0	*Normal*	*Abnormal*	
2	36			Trace	Normal	Normal	
3	211				Normal	Normal	
	29	20					
4	32		5.0	Trace		Normal	
5	118		42.0	0.9	Abnormal	Abnormal	
6	119			1.8		Abnormal	
7	150			2.8			
	35	4					
8	36		4.7	Trace			
9	56		12 0	3.0		Abnormal	Autopsy—Fat necrosis, P. necrosis
	26	4					
10	93		10	4.6		Abnormal	
	36	2					
	73	4					
11	82					Abnormal	
12	73		15.0			Abnormal	
13	67				Normal	Normal	
14	43		4.9			Abnormal	
	15	1					
15	31		6.1	5.6			
16	94						
	22	1					
17	36		2.9	Trace	Normal	Normal	
18	31		4 8	3.4	Normal	Normal	
19	55		8 8	1.5		Normal	
20	136			2 8	Normal		
	23	3					
21	51		11.0	14.0	Abnormal	Abnormal	
	42	2					
22	45		11.0	5.0		Abnormal	
23	269			Trace		Abnormal	Serum lipase 14.2*
	58	1					Serum lipase 4 1
24	88		2.2	2.7			
25	38		11.6	8.3			
26	80		14.0	1.2		Abnormal	
27	94			3.0			F.U. 14 yrs. uneventful
28	40		6.0	20.0		Abnormal	F U. 6 yrs. uneventful

*The elevation of the lipase and amylase was about ten times the normal. This patient had two bouts of pancreatitis in succeeding years

SERUM AMYLASE IN PATIENTS WITH STONE IN THE COMMON BILE DUCT

The amylase was above normal in 28 of 40 patients (70 per cent) with stone in the common duct. The surgeon examined the pancreas in 19 of these 28 patients. He found induration, enlargement or fat necrosis in 15 (79 per cent). As in acute pancreatitis without common duct stone, the decline of serum amylase was usually rapid.

In 26 patients (65 per cent), measurable amounts of bilirubin were found in the serum.

Pancreatic function tests were carried out in 12 patients; 8 were normal (66 per cent). The association of pancreatitis with common duct stone is frequent. The generally accepted cause of this complication is the entrance of bile into the pancreatic duct, the so-called common channel theory. In support of this time-honored conception is the fact that in human cholangiograms the contrast medium injected into the common bile duct occasionally enters the pancreatic duct. Leven[37] saw the pancreatic duct in 23 per cent of 91 cholangiograms. In a few instances, actual blockage of the opening of the pancreatic duct by a stone in the ampulla may account for an elevated amylase. The follow-up experience indicates that removal of the stone results in permanent cure in the larger number of patients.

TABLE 19. NORMAL SERUM AMYLASE IN PROVED CASES OF COMMON DUCT STONE

No.	Serum *Amylase*	Serum *P'tase*	Serum *Bili.*	Pancreatic Function Test	Condition of Head of Pancreas at Operation	Remarks
1	13	21 0	1.6		Normal	
2	16	7.9	9.4	Abnormal	Normal	
3	30	7 3			Abnormal	
4	28			Normal		
5	22				Abnormal	
6	17				Normal	
7	12	4.0	3 2		Normal	
8	16		5 1		Abnormal	
9	12	6 0	12 5		Normal	
10	15		5 4			F.U. 6 yrs. uneventful
11	23	8 4	6.3			Serum lipase 1.2 (normal)
12	12		8 1			F.U. 5 yrs uneventful

The causal relationship between gallstones and pancreatitis is one of several good reasons for advising cholecystectomy, once the diagnosis of gallstones has been established. Common duct stones, suppurative cholecystitis, cholangitis, perforation of the gallbladder and carcinoma of the gallbladder are other possible complications of stones in the gallbladder. Not too rarely, these complications occur late in life, forty or more years after the disease first made its presence known, when the operative risk is potentiated, and the choice of surgeon and hospital is not optional.

TABLE 20. NORMAL SERUM AMYLASE IN DUODENAL ULCER

No.	S.A.	Symptoms of D.U.	X-ray Evidence of D.U	Operation	Remarks
1	30	+	+	Partial gastrectomy	Pancreas normal
2	21	+	+	None	
3	20	+		Suture	Perforating ulcer
4	12	+	+	None	
5	22	+	+	Suture	Perforating ulcer
6	13	+	+	None	
7	30	+		Partial gastrectomy	Ulcer penetrating into head of pancreas
8	25	+		Partial gastrectomy	
9	26	+	+	Partial gastrectomy	
10	17	+		Suture	Perforating gastric ulcer
11	26	+	+	None	
12	20			Suture	Perforating duodenal ulcer
13	19	+		Suture	Perforating duodenal ulcer
14	19	+		Suture	Perforating duodenal ulcer
15	30	+	+	None	
16	17	+	+	None	
17	26	+	+	None	
18	29	+	+	None	
19	17	+	+	None	
20	21	+		Partial gastrectomy	Inflammation about head pancreas
21	23	+	+	Partial gastrectomy	Penetrating ulcer, firm head pancreas
22	26	+	+	None	
23	26	+	+	Partial gastrectomy	
24	28	+	+	Partial gastrectomy	Pancreas normal
25	30	+	+	Partial gastrectomy	
26	19	+		Perforating duodenal ulcer	
27	17	+	+	None	

TABLE 21. ELEVATED SERUM AMYLASE IN DUODENAL ULCER

No.	S A.	Symptoms of D.U.	X-ray Evidence of D.U.	Operation	Remarks
1	46	+	+	None	
2	74	+	+	None	
3	42	+	+	Partial gastrectomy	Ulcer adherent to pancreas
4	65	+	+	None	
5	31	+	+		
6	34	+	+	None	
7	33	+	+	Partial gastrectomy	Ulcer penetrating into pancreas
8	31	+	+	Partial gastrectomy	
9	59	+	+	Partial gastrectomy	
10	129	+	+	Partial gastrectomy	Ulcer adherent to pancreas
11	89	+	+	Partial gastrectomy	Ulcer adherent to pancreas
12	48	+	+	Partial gastrectomy	Ulcer post. wall, prepyloric
13	56	+	+	Partial gastrectomy	Ulcer adherent to pancreas
14	157	+	+	Partial gastrectomy	Ulcer adherent to pancreas
15	53	+		Partial gastrectomy	Ulcer pylorus penetrating pancreas
16	51			Repair of prepyloric perforating ulcer	
17	32			Repair of perforating duoden. ulcer	
18	157	+	+	Partial gastrectomy	Ulcer adherent to pancreas
19	56	+	+	Partial gastrectomy	Perforating ulcer sealed by pancreas
20	41	+	+	None	
21	151	+	+	Partial gastrectomy	Penetrating ulcer
22	65	+	+	Drainage subphren. abscess	Perforating ulcer
23	33	+	+	Partial gastrectomy	

SERUM AMYLASE IN DUODENAL ULCER

As the posterior and inferior surfaces of the duodenal bulb are contiguous with the head of the pancreas, penetration of a posterior ulcer may result in sufficient inflammatory swelling of the pancreas to interfere with the outflow of pancreatic juice and thus raise the serum amylase level.

Comfort and Osterberg[74] report serum lipase determinations in 102 cases of duodenal and 3 cases of gastric ulcer. In only 7 was the lipase elevated, and in all the ulcer had penetrated into the pancreas. The lipase was also elevated in 2 of 31 cases of carcinoma of the stomach, and here also the tumor had invaded the pancreas.

The serum amylase is usually normal in duodenal or gastric ulcer. An elevated serum amylase in a patient with chronic duodenal ulcer is an argument in favor of partial gastrectomy.

SERUM AMYLASE IN CHRONIC NEPHRITIS

The elevation of serum amylase in kidney disease in obviously due to its dimished elimination. The practical value of this test would have to be determined on a larger series.

Whether the glomeruli alone participate in the elimination or whether there is tubular secretion or reabsorption of amylase is not known.

From his studies in experimental uranium nephritis, Fitz[78] concluded that the amylase excretion test was similar but less delicate than the 'phthalein test.' Geyelin[79] found that the amylase and phenolsulfonphthalein excretion were comparable in human kidney disease. Heifitz et al.[80] observed that the serum amylase was elevated in 70 per cent of 111 cases of renal insufficiency.

Recently a patient suffering from chronic nephritis, hypertension and urea retention developed upper abdominal pain, leukocytosis and an elevated serum amylase. Exploration revealed a subcapsular hemorrhage of the liver instead of the expected acute pancreatitis. The elevated serum amylase was apparently due to retention.

TABLE 22. ELEVATED SERUM AMYLASE IN KIDNEY DISEASE

No.	S.A.	CLINICAL FEATURES	UREA *Nitrogen* *mg. %*	SERUM *Phosphatase* *mg. %*	REMARKS
1	43	Chronic glomer nephritis	185	11.7	Autopsy
2	85	Chronic glomer. nephritis	23	5 7	Autopsy
3	32	Chronic glomer. nephritis	15		
4	82	Nephrosclerosis	57		Autopsy
5	146	Chr. glomer. nephritis	110		Autopsy

SERUM AMYLASE IN SALIVARY GLAND DISEASES

A considerable part of the amylase in the serum is furnished by the salivary glands. In dogs, Pratt[12] and associates observed high serum amylase values when little or no pancreatic parenchyma remained. When there is obstruction of the salivary duct system by tumor,

calculus, or inflammation, reabsorption increases sufficiently to raise the amylase level in the serum.

Recently, Wolman and his associates[81] reported a series of amylase tests in 101 cases of adult mumps. An elevation occurred during the first week which faded during the second week. Zelman[82] found that 73 per cent of mumps cases have an elevated amylase. In doubtful cases of sialadenitis, the test should have diagnostic value.

TABLE 23. ELEVATED SERUM AMYLASE IN SALIVARY GLAND DISEASE

No.	S.A.	CLINICAL FEATURES AND REMARKS
1	34	Parotitis
2	35	Mumps
3	49	Tumor of the parotid (composite)
4	56	Swelling of submaxillary gland—removal of calculus from duct
5	92	Mumps

SERUM AMYLASE IN MISCELLANEOUS ABDOMINAL DISEASES

Lewison[83] found that the serum amylase was normal in 94 per cent of 720 patients who were not afflicted with pancreatic, salivary, or biliary tract disease.

In our series of miscellaneous operated abdominal cases (Table 24), the serum amylase was usually below 30, the upper limit of normal. Slight elevations are not always easy to explain.

TABLE 24. SERUM AMYLASE IN MISCELLANEOUS ABDOMINAL DISEASES

No.	Serum *Amylase*	*P'tase*	*Bili.*	*Ceph. Floc.*	CLINICAL FEATURES AND REMARKS
1	20		11.	4+	Jaundice, no operation, hepatitis, normal P. Function Test
2	23		15		Jaundice, ca. hepatic duct
3	25	6.7	11 4		Jaundice, hepatitis, no operation
4	24	6 0	17.	3+	Jaundice, hepatitis, no operation
5	17	10 0	18.	3+	Jaundice, hepatitis, no operation
6	26	20	19.		Jaundice, hepatitis, no operation, normal P. function test
7	23		Trace		Jaundice, epigastric pain, stenosis rt. hepatic duct, normal P. function test

TABLE 24 (*Continued*). SERUM AMYLASE IN MISCELLANEOUS ABDOMINAL DISEASES

No.	Serum *Amylase*	*P'tase*	*Bili.*	*Ceph. Floc.*	Clinical Features and Remarks
8	23	10	4.5	0	Jaundice, hepatitis, no operation, normal P. function test
9	10	9.7	4.7	4+	Jaundice, hepatitis, no operation
10	23		10.8		Jaundice, R.U.Q. pain, stenosis of common bile duct, no operation
11	11		26		Jaundice, ca. ovary metast. region pancreas
12	34	39	1.6	0	Hepatitis, cholangitis, exploratory, jaundice
13	32	7.0	5.7	4+	
14	47		10.4		
15	20				
16	27				
17	21				
18	18				Pain ant. chest, myoc. in infarction, no operation
19	27				Epig. pain, dissect. aneurism, no operation
20	8				Epig. pain, amebic hepatitis, ameb. stool, no operation
21	16				Abd. pain, distention, dilated small intestine
22	15				Left abd. pain, ca. sigmoid
23	17				
24	16	9.6	7.2		mal
25	33		2.3		
26	36				tion
27	34				
28	9				
29					
30	13				Gland enlarged, autopsy—Hodgkins disease
31	24				Acute appendicitis
32	21				Epig. mass, normal pancreatic function test, retroperitoneal sarcoma
33	18				Acute intestinal obstruction
34	28				Large liver, spleen, no operation, cirrhosis of liver
35	31				Acute appendicitis
36	75				Partial gastrectomy, small ulcer, 100% gastric retention and vomiting
37	35				Mid. abd. mass, retroperitoneal sarcoma

In patient No. 32, disease of the pancreas was suspected.

CONCLUSIONS

Our knowledge of the pathologic physiology of the pancreas has been furthered by chemical laboratory procedures.

The minimal ferment activity of the pancreatic juice by the Free and Myers method after mecholyl stimulation in nonpancreatic disease is 4 mg. of reducing sugar for amylase, 50 mg. of nonprotein nitrogen for protease, and 8 cc. of 0.1 normal butyric acid for lipase.

The determination of ferment concentration in the pancreatic juice is helpful in the diagnosis of obstructive jaundice, chronic pancreatitis and sprue.

As the pancreas has a large functional reserve, marked diminution of ferment concentration indicates widespread disturbance. Rarely, autonomic imbalance may alter ferment concentration through abnormal vagal influence.

In nonjaundiced patients, the determination of fecal fat is helpful in the diagnosis of pancreatic disease and in ascertaining the effect of orally administered ferments.

An elevated serum amylase is diagnostic of acute inflamation or edema of the pancreas and thus serves to differentiate this from other acute abdominal conditions.

The serum amylase may also be elevated in duodenal ulcer penetrating into the pancreas, in inflammation of the salivary glands, and in advanced kidney disease.

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